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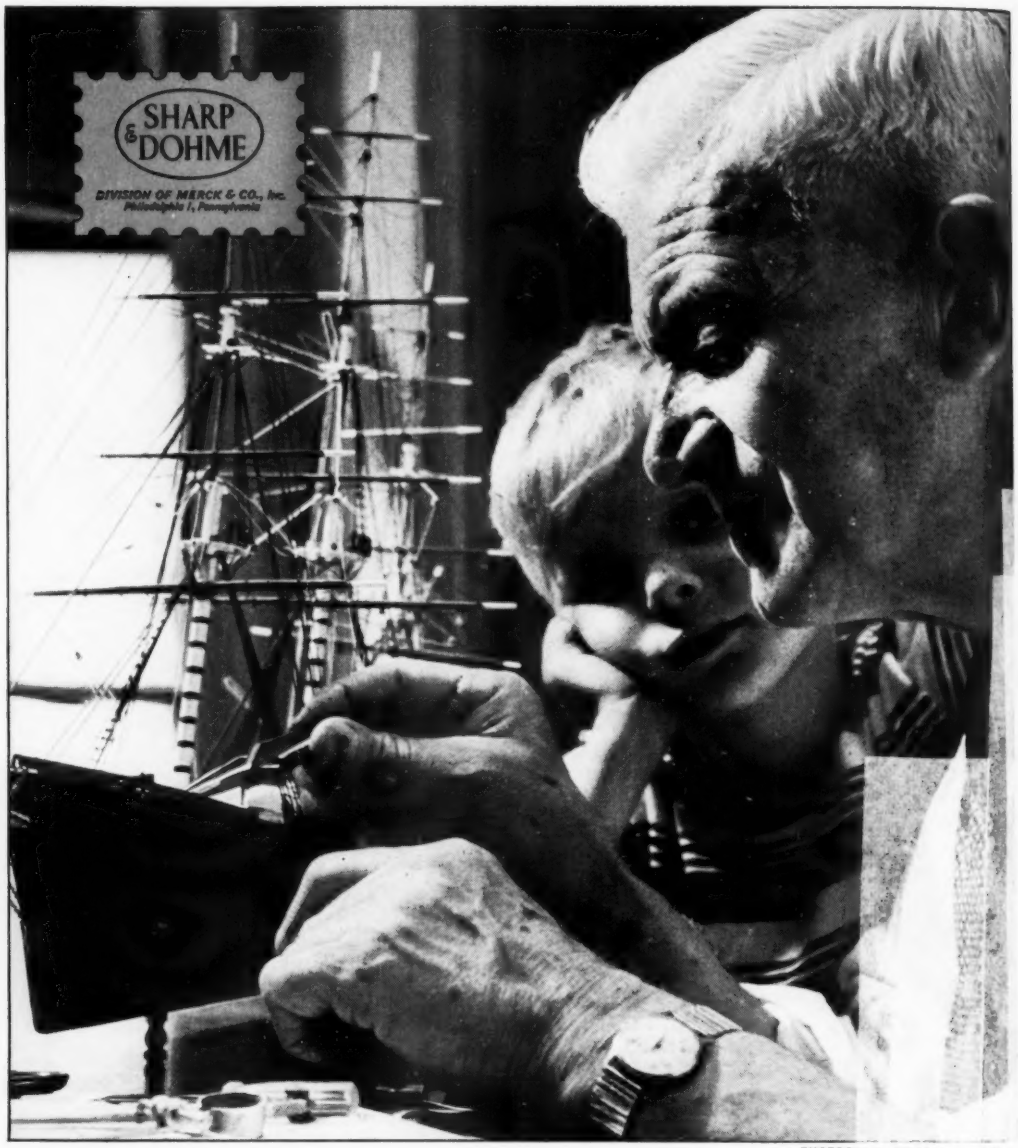

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• GROWTH RETARDATION

Question: I would greatly appreciate your suggestions as to therapy in the case of a 15 year old schoolboy whose height is 56½ inches and who weighs 141 pounds. His temperature is 98.6° F., pulse 84. His mother says he has stopped growing and she wonders what can be done to make him grow. She says he plays a lot and does not get tired. Physical examination reveals an obese boy. His hands are shaped like spades. He appears very healthy. His heart is slightly irregular at times. His blood count is normal. Urinalysis shows urine to be acid with a trace of albumin and a large number of pus cells. What would you suggest in the way of treatment?

M.D.—Michigan

ANSWER: The problem posed is difficult to answer because of the meager information that is supplied. We know that this boy is too short; we do not know whether he has delayed sexual and somatic development. His past history is not given, so we cannot tell whether he has been subject to disease conditions which may have retarded his development. One of the most helpful procedures would be to obtain x-ray films of his wrists in order to evaluate his bone age. From this evidence one would be able to tell whether the patient is really dwarfed or just delayed in his development.

The causes of dwarfism are many, and a detailed discussion of them is beyond the scope of this answer. A good summary can be found in the recently published text by Dr. Lawson Wilkins entitled "The Diagnosis and Treatment of Endocrine Disorders in Childhood and Adolescence," published in 1950 by Charles C Thomas, Springfield, Illinois. Dr. Wilkins lists in his table on page 120 the following main causes for dwarfism: (1) bone diseases, (2) nutritional or metabolic disorders, (3) circulatory disorders with anoxemia, (4) endocrine disturbances, (5) delayed adolescence with retarded growth, (6) primordial or genetic dwarfism (constitutional) and (7) unclassified types. The treatment is obviously going to depend on the cause of the dwarfism.

From the evidence that is given, however, it is quite clear that this boy is also very obese, and this in itself could be one of the main factors in retarding his growth. He should be placed on an 800 calorie, high protein, low fat diet without added carbohydrate. It should be stressed that he eat 3 meals a day, but only 3 meals a day. He should take plenty of water in order to help with the problem of burning his own fat. In addition to this he should be placed on some anorexic drug such as DEXAMYL®. He should be started on 2.5 mg. one hour before breakfast, and this should be increased at intervals of about 1 to 2 weeks so that he takes it before breakfast, before lunch, and even before dinner, and gradually steps up the dose so that he may take as much as 15 or 20 mg. after some months. It is of great importance to recognize that these patients quickly develop tolerance to such drugs, and unless the dose is raised at frequent intervals they will fail to have the suppression of appetite and to be able to adhere to their program. A transient disturbance in the ability to be able to sleep can be ignored, as it wears off in a day or two. When the dosage of medication gets sufficiently large, it can be eliminated for a few days and then the patient will recover his tolerance to it and can be started at small doses again.

It has been our impression that individuals who are gaining weight excessively do not develop very rapidly because they store in their fat the steroids produced by their gonads, and thus these substances are not available to cause the developmental changes. It is surprising how rapidly many of these patients begin to adolesce and develop as soon as they are put on a reducing regimen and begin to lose weight. According to the tables given by Dr. Wilkins, the ideal

(Continued on page A-40)

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weight for a boy of 15 years would be 101 pounds and the ideal height 62½ inches. For his current height, however, the boy should weigh approximately 75 pounds, so he is nearly twice as heavy as he should be. The amount of weight he should lose will depend somewhat on how rapidly he grows, assuming that he is still capable of growing and that his epiphyses have not closed.

The other point that needs observation is apparent in the question submitted: a study of the possibility of chronic renal disease. This may also be responsible for retarded development. The question of a chronic acidosis is raised by the fact that the urine is said to be acid. I think this problem should be followed up as soon as the patient has begun effectively to lose weight.

Once the weight has been reduced to approximately normal and the renal status has been evaluated, the problem will be clarified. If the boy still shows evidence of delayed growth, then other factors including the endocrine disturbances can be investigated.

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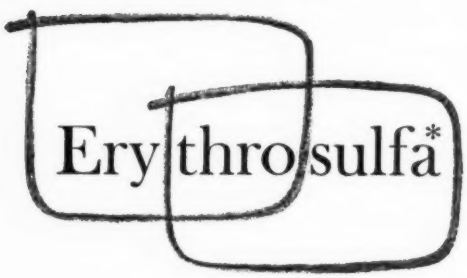

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• RECURRENT VOMITING IN YOUNG CHILD

Question: A patient, 3 years of age, female, has had weekly recurrent attacks of vomiting since December 1952. When vomiting ensues, it cannot be stopped by any antivomitive medicine, but after 3 to 5 days it will stop by itself without any medical aid. She has been treated by several pediatricians and was given Emetrol, pyridoxine, LUMINAL®, sodium citrate, chloral hydrate, bromide and GYNERGEN® injection, but the vomiting still persisted.

Laboratory examination shows no evidence of any pathologic changes in the blood and the stool shows no evidence of any parasite. The vomiting is always accompanied by slight fever ranging from 38° C. to 39° C. The vomiting has always appeared in cycles at weekly intervals. Up to the present date, 7 months duration, the vomiting still recurs. I would appreciate any suggestions or treatment you may be able to offer for suppressing entirely the recurrence of the vomiting.

M.D.—Philippines

ANSWER: Intractable, regularly recurring vomiting in a child 3 years old should raise the suspicion of a cerebral factor, a functional disorder and organic obstruction. Cerebral causes usually, although not always, should be fairly easy to eliminate in the absence of any evidence of increased intracranial pressure.

The commonest functional vomiting in young children is known as "cyclic vomiting," and behaves very much as the vomiting does in the patient in question. Such vomiting is accompanied by ketosis, and sometimes the attacks can be shortened by the intravenous administration of a 5 per cent solution of glucose in water or an isotonic solution of sodium chloride.

Organic obstruction such as that caused by adhesions or bands, and that due to anomalies such as malrotation of the colon, may be demonstrable by roentgenoscopic examination with an opaque medium. Perhaps the first procedure would be careful examination of the colon to make sure that malrotation is not present. Occasionally, study of the stomach and duodenum with the aid of barium or opaque oil will give a clue. If the evidence is fairly strong in favor of an organic obstruction, proof may not be forthcoming until laparotomy has been performed.

Experimental Studies on the Use of Large Volumes of Saline in the Therapy of Traumatic Shock

SANFORD M. ROSENTHAL*

National Institutes of Health, Bethesda, Maryland

This article comprises a summary of the work done in our laboratory on traumatic shock in laboratory animals. The underlying fluid and electrolyte changes, the relation of hemodynamic changes to mortality, and the therapeutic results with saline solutions, blood and plasma are presented. Standardized trauma from burns, tourniquet application or hemorrhage is employed, and evaluation of therapy is made primarily on a basis of mortality.

SANFORD M. ROSENTHAL

THE studies to be described were carried out by Dr. Herbert Tabor, Dr. R. Carl Millican and myself at the National Institutes of Health. During the past 12 years over 15,000 mice have been used, for it has been found that in spite of careful standardization, it is only by large numbers that the biologic variations inherent in this type of experiment can be overcome.

It is essential to define the type of shock employed; it is a lethal degree of trauma from burns or from injury to the extremities, and is associated with considerable fluid loss in the form of swelling of the injured areas. Our results do not apply to forms of shock not associated with extensive fluid loss. The limitations of this address make it necessary to restrict the presentation to a review of our work, so that it will not be possible to refer to the extensive investigations by others in this field.

It is not to be inferred that our results can be applied quantitatively to man, but I believe the basic principles involved merit clinical consideration.

*Chief, Section on Pharmacology and Toxicology, National Institute of Arthritis and Metabolic Diseases, National Institutes of Health, Bethesda, Maryland.

Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

Methods

By the use of simple technics it has been possible to employ large numbers of animals under highly standardized conditions, so that one lethal dose of trauma is employed and our results are quite reproducible. This is very important because the field of experimental shock has been often confused by results obtained on small numbers of animals under conditions improperly standardized.

Burn shock is produced by immersion of the shaved mouse to the axilla in water at 70° C. for 5 seconds. This produces second and third degree burns of approximately two-thirds of the body surface. The animals are etherized only during the induction of trauma, so that the experiments are not complicated by prolonged anesthesia.

Tourniquet shock is produced by applying rubber bands high on the thighs of mice for a period of 2 hours (Figure 1). While the

FIGURE 1. Application of tourniquets to the thighs of mice.

bands are in place the animals show no symptoms of shock, but soon after removal circulatory collapse develops and death occurs in 12 to 24 hours in untreated animals.

Hemorrhage has also been studied but we have been unable to produce delayed hemorrhagic shock in mice, so these experiments are confined to acute death from blood loss. We have devised a "bleeding apparatus" whereby measured hemorrhage can be simultaneously carried out on 40 animals at one time (Figure 2). Simultaneous comparison of alternate groups is, we believe, an important part of our standardization.

The standardization of the trauma so that one lethal dose is administered is also important, for if two lethal doses are employed (as by tourniquet application to all 4 legs) we have found no therapy effective in bringing about survival. This is a challenge to the investigator, for when more is known about the basic mechanisms involved, it should be possible to extend the effectiveness of therapeutic measures in shock.

Therapeutic Results

Early in the course of our work it was found that isotonic sodium solutions were capable of preventing death from the 3 forms of trauma described. This is a specific effect of the sodium ion; it has been shown that all sodium salts behave similarly, while potassium, instead of being beneficial, is actually harmful. Fluid replacement as well as sodium

is important, and administration of sodium in solutions of isotonic strength yielded the most effective therapy.

One of the reasons for failure of saline therapy in the hands of other investigators is that insufficient quantities were used. We have found that when 5 per cent of the body weight (B.W.) of 0.9 per cent sodium chloride was administered (1 cc. per 20 gram mouse), only half of the animals could be saved. When the amount was increased to 10 per cent B.W., approximately three-fourths of the mice survived, and with 15 per cent B.W., 90 to 95 per cent of the mice survived.

When these large amounts of saline were used they were effective when given orally or intraperitoneally, as well as intravenously. A good therapeutic effect could be demonstrated even when therapy was delayed for 6 hours after the onset of shock. As added proof for the importance of sodium, similar amounts of isotonic glucose or of crystalline serum albumin suspended in glucose had relatively little effect on survival—only a delaying action.

Serum or plasma or an ultrafiltrate of serum containing no proteins showed an effect which could be duplicated to a large degree by an equal volume of saline, suggesting that the beneficial action of plasma in shock is to a considerable extent due to the sodium and fluid that are contained in it. An exception to this is hemorrhage, where whole blood or red cells suspended in saline were appreciably superior to plasma or to saline.

Figures 3 to 6 illustrate some of these results. When other therapies are compared with saline, all volumes employed are usually limited to 5 per cent of body weight because this amount of saline will bring about a 50 per cent survival response, which is the most satisfactory response for purposes of comparison—to detect whether another therapy is better or worse.

When mouse whole blood and mouse plasma were compared in the treatment of burn or tourniquet shock, no difference in survival value could be shown, so that in our laboratory studies we have no proof that whole blood is superior to plasma except in the treatment of hemorrhage.

Comparisons of plasma with equal volumes

FIGURE 2. Apparatus for production of standardized hemorrhage in large numbers of mice.

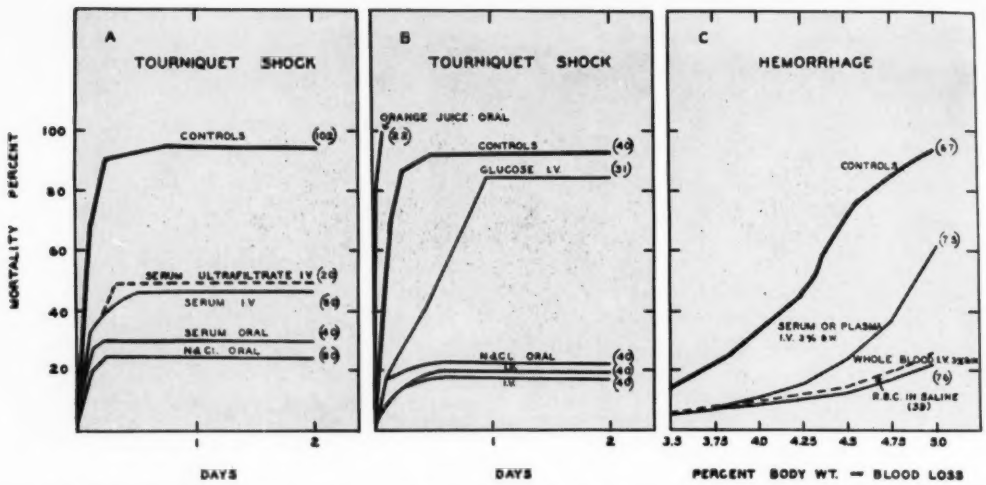

FIGURE 3. Survival response of various therapeutic measures. A. Similar response of mouse serum and a protein-free ultrafiltrate of serum, given intravenously in single doses of 10 per cent body weight. B. Effectiveness of large doses of saline (10 per cent body weight) by all routes of administration. Ineffectiveness of dextrose. C. Superiority of whole blood over plasma in hemorrhage. All curves are composites of several experiments, and numbers in parentheses signify numbers of mice used.

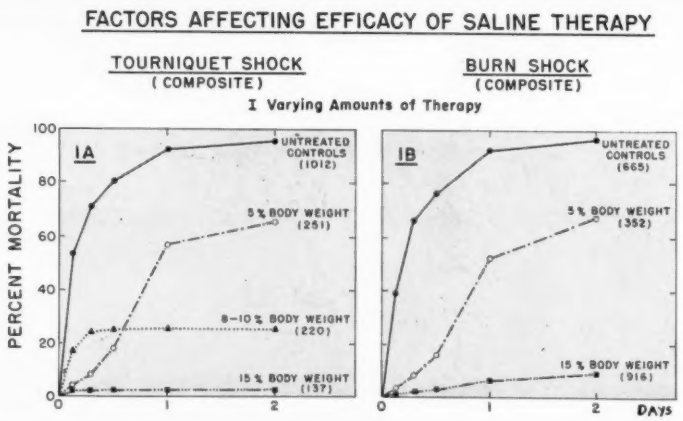

FIGURE 4 (I): Comparison of therapies in shock. The relation of dosage of saline to survival response.

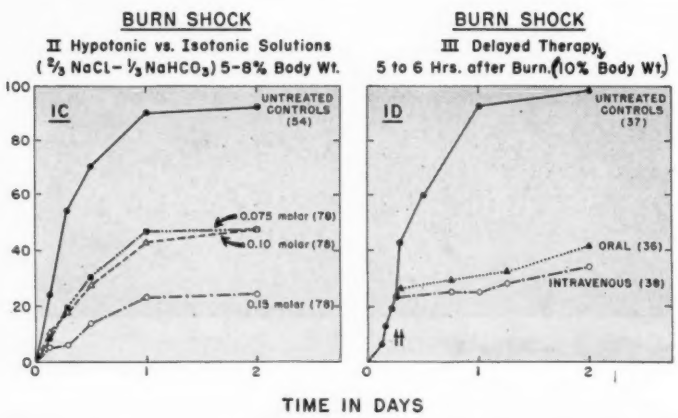

FIGURE 5 (II). Isotonic sodium solutions are superior to hypotonic solutions. (III). Saline therapy is effective when administered 6 hours after onset of shock.

of saline did not show any superiority of plasma when therapy was administered in one or two doses. Since this is contrary to clinical experience, an extensive study under other conditions was carried out. Swingle and coworkers have shown that in dogs, multiple injections of plasma were superior to single injections, equal total quantities being employed in both cases. We have likewise demonstrated in mice that extending therapy with plasma over 7 or 8 hours does show some increase in effectiveness, while this increased benefit was not obtained with saline. A quantitative comparison under these conditions revealed that increasing the saline to a volume 50 per cent greater than that of plasma was necessary to bring about equal survival from these two therapies (Figure 7).

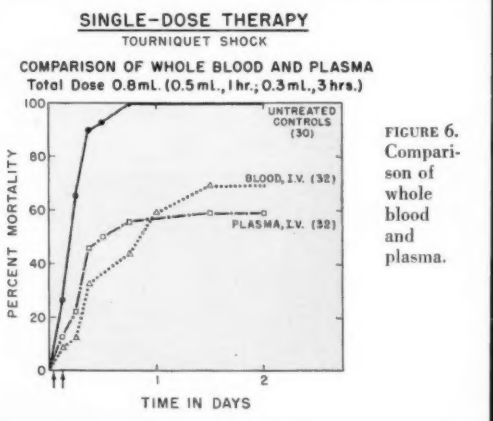

FIGURE 6. Comparison of whole blood and plasma.

Evaluation of Therapy

Let us turn now to a possible explanation of some of the differences between laboratory results and clinical practice. Saline has been used in the clinic for over 75 years in the treatment of shock and there are still conflicting opinions of its value. I believe there are 3 chief reasons for this: (1) Insufficient amounts have been used; clinical therapy has been largely intravenous, and rarely over 3 to 5 per cent of body weight (2 or 3 liters of saline to an adult) has been used. As you have seen, in the laboratory this is an ineffective dose; (2) the difficulty of appraising the value of therapy in individual clinical cases; (3) the criteria on which the value of therapy is judged have been largely limited to the acute response of blood pressure, blood volume and other hemodynamic changes which are present in shock. Millican, Tabor and I have obtained evidence that the circulatory response may not be a valid index of the success of therapy; the results may be misleading when compared with the ability of therapy, particularly saline solutions, to bring about survival of the animals from shock.

We have employed hematocrit, plasma protein concentration, and bleeding volume (an index of blood volume) as criteria of circulatory changes in the shocked mouse. It was found that whole blood or plasma intravenously restores bleeding volume to values slightly above normal immediately after ad-

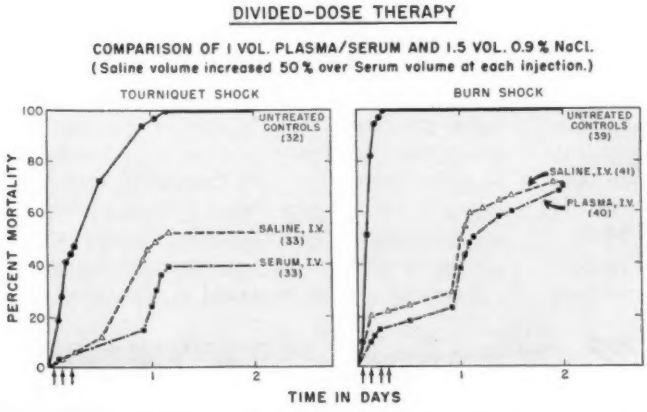

FIGURE 7. When therapy is administered over a period of hours, plasma is superior to saline, but similar survival rates were obtained when the dose of saline was increased 50 per cent.

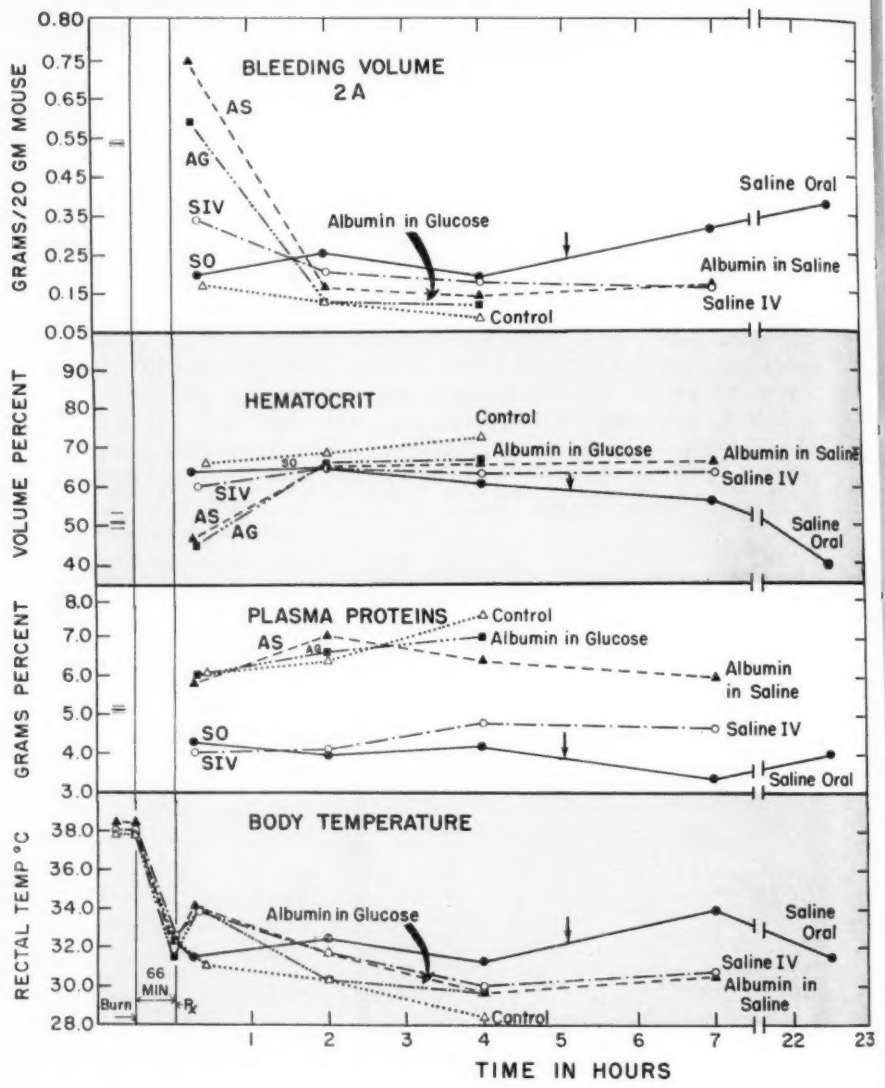

FIGURE 8A. Hemodynamic effects in burned mice following single doses of therapy. Responses from albumin in glucose (AG), albumin in saline (AS), saline intravenously (SIV) and saline orally (SO).

ministration, and with plasma the elevated hematocrit is lowered to normal. Saline intravenously elicits a circulatory response of lesser magnitude, and saline orally has very little early effect. However, on a basis of mortality these therapeutic measures were of equal effectiveness under the conditions employed.

The explanation lies in that the acute effects from colloids are to a large extent transitory, while the circulatory responses from saline therapy develop slowly, so that it is only by following these changes over a period of hours that the effectiveness of large volumes of saline in restoring the circulation may be brought out (Figure 8B). Plasma proteins are invariably lowered by saline therapy, and cannot be accepted as a criterion of therapy.

Likewise a false appraisal of the value of

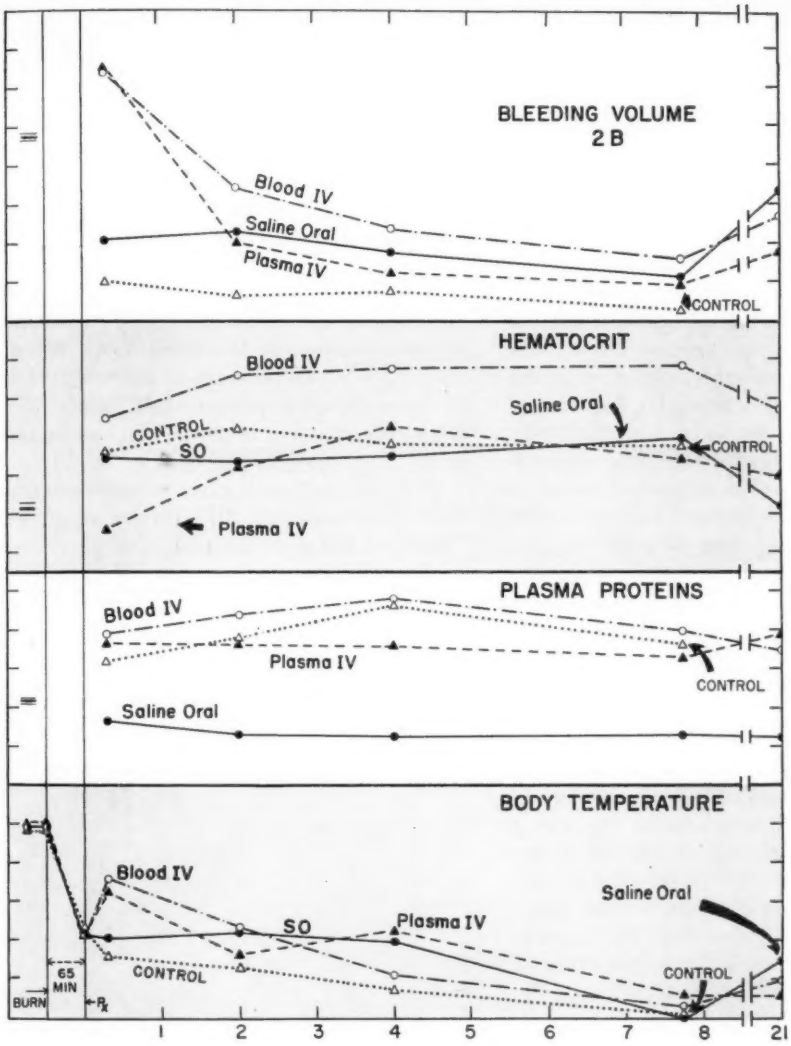

FIGURE 8B. Response following whole blood or plasma, and saline orally. Single doses of 1 ml. given 65 minutes after trauma. In the first column of each chart the symbol represents values in normal mice.

colloids, administered in the absence of sodium salts, may be obtained, for albumin administered in glucose solutions brought about acute circulatory responses equal to that of plasma; however, by following these changes over a period of time it was found that bleeding volume and hematocrit values following albumen in glucose after a few hours approached those of the shocked mice that received no treatment (Figure 8A).

Therefore, circulatory changes as an index of the effectiveness of therapy would seem to be reliable only if followed over a period of hours after the administration of therapy.

Mechanism of Saline Therapy

Blalock and Duncan first showed in dogs with tourniquet shock that the extra fluid

which accumulated in the injured legs (in the form of swelling) amounted to 5 per cent of the animal's weight, and that a hemorrhage of this extent would be fatal. Tabor and I found a similar fluid accumulation in mice, and by analyzing the injured areas showed that not only was sodium carried in by this fluid, but also that the injured tissues released potassium, and additional sodium entered to replace this potassium. The release of this potassium into the rest of the body explains to some extent the sensitivity of the shocked animal to potassium. The magnitude of the sodium need in shock was studied by giving an excess of saline therapy and determining the amount that was retained in the body; a marked sodium retention was demonstrated, and approximately 15 per cent of body weight in terms of isotonic saline was retained during the first 48 hours following trauma (Figure 9).

For a long time we were unable to explain why the animal requires 10 to 15 per cent of body weight of saline for optimum therapy when only a third of this (5 per cent) was accounted for in the injured areas of *untreated* mice. Quantitative studies of the distribution of administered fluid provided the answer. Previous estimates of the maximum fluid loss of 5 per cent B.W. had been derived from untreated animals. When treatment amounting to 6 to 18 per cent of body weight was given, a small part of this served to correct the dehydration of the uninjured tissues, but the major portion of the administered fluid was recovered in the injured areas in the form of further swelling. This accumulation occurs rapidly, within 2 hours after the fluid is injected, and occurs to the same extent with plasma therapy as with saline (Figure 10). It is significant that no edema of the viscera or other uninjured tissues occurred with these large volumes of therapy.

The demands of the injured tissues to swell must therefore be met before the dehydration of the uninjured tissues can be corrected, and it is believed that this dehydration may be an important factor in death from shock. Large volumes of sodium-containing fluids are thus a basic requirement for good treatment, whether or not blood or plasma is also used. The additional swelling of the injured areas which results from this therapy should not be a deterrent to its use.

Conclusions

The optimal amount of therapy of isotonic sodium solutions in traumatic shock in animals is 10 to 15 per cent of body weight in 24 hours. Blood or plasma alone cannot fulfill this requirement, in terms of fluid and sodium need.

Water or glucose solutions in water are relatively ineffective in the therapy of shock. Potassium solutions are toxic.

The acute hemodynamic responses may not

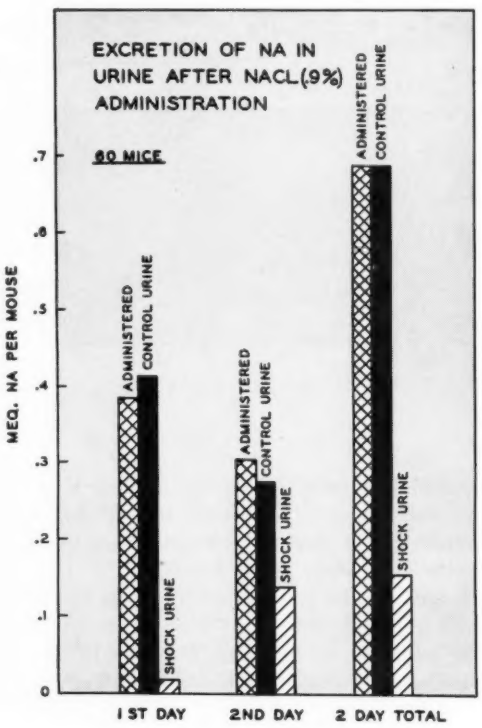

FIGURE 9. Sodium excretion in tourniquet-shocked mice after administration of 15 per cent of body weight of saline the first day and 11 per cent the second day. Practically no sodium was excreted the first 24 hours, and 28 per cent of the total was excreted in 48 hours.

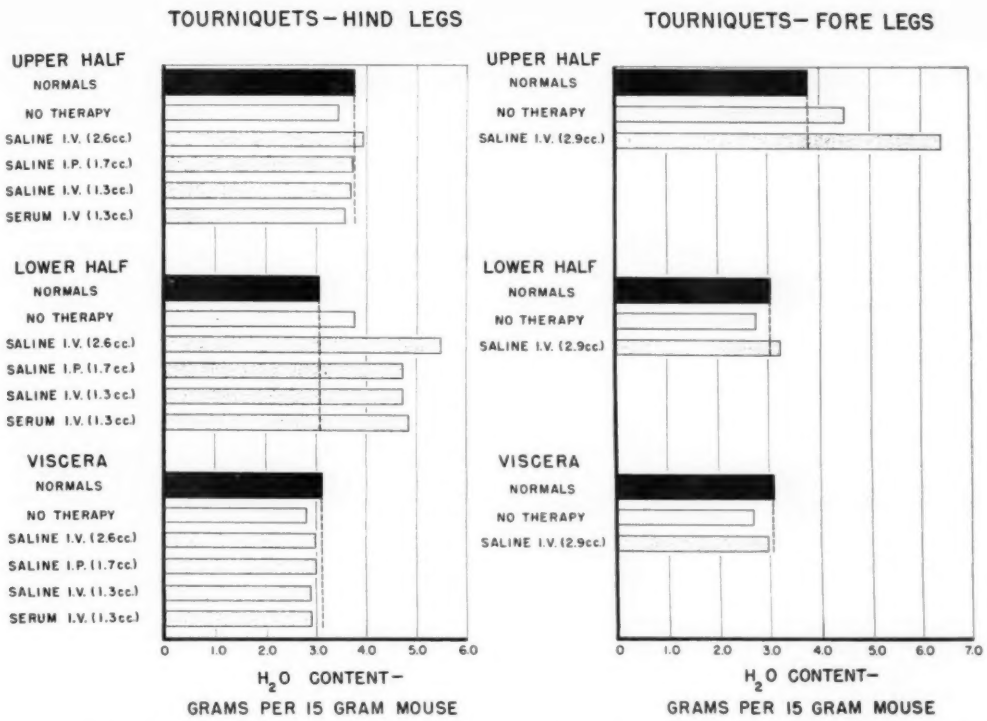

FIGURE 10. Water content of the upper half of the body, lower half of the body, and viscera of normal mice and of mice with tourniquet application.

be reliable criteria of the effectiveness of therapy. The beneficial effects of saline on the circulation may not be detected for several hours.

Oral therapy with saline solutions is quite effective in animals, and when possible should be used along with parenteral therapy to supply the large amounts needed.

In mass casualties or in other situations where intravenous therapy is not immediately available, oral saline therapy offers the possibility of a valuable therapeutic measure.

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Tumors of the Colon

GEORGE W. CRILE, JR. AND RUPERT B. TURNBULL

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Today's surgeon must be versatile to carry out several operative procedures for tumors of the rectum. Miles' operation is best for cancer, while sphincter-preserving procedures are best for large diffuse benign tumors or those containing noninvasive cancer. Adequate biopsy must be obtained from nonmalignant tumors before making the decision to preserve the sphincters.

GEORGE W. CRILE, JR.

RUPERT B. TURNBULL

TREATMENT of tumors of the colon has always been a controversial subject, because surgeons have lined up almost on chosen sides on certain issues. The exponents of one operation have let it be known that that operation is the only one ever to be used, while others have said, "You should never use that operation, you should use this other operation." So there has been a great deal of confusion in the minds of the physicians of this country, because each of these surgeons has perhaps mastered his own technic of dealing with a certain problem but has not always taken into account some of the advantages of other procedures with which he may be unfamiliar.

We believe there is a place for each of these operations, and I am referring now particularly to those for tumors of the colon located in the low sigmoid and upper portion of the rectum. The surgeon responsible for the care of these patients should be prepared to use each type of operation selectively, and the final decision as to which should be employed often must be deferred until all the factors pertaining to the tumor itself are known, i.e., until the time of operation; also, consideration must be given to the adaptability of the patient to the procedure.

We think we can best present this problem by discussing individual cases, and the first patient is Mr. S., who had multiple carcinomas and polyps of the rectum and who was firmly opposed to colostomy. Dr. Turnbull, will you describe this case?

DR. RUPERT B. TURNBULL: There were multiple polyps and multiple carcinomas (Figure 1). I generally tell these patients before operation that they are to have an artificial opening or colostomy. By the time we see them, they usually expect that that is what is to be done. However, this man was very upset by the diagnosis, and although I mentioned colostomy in the conversation, I didn't stress it

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and I don't believe that he understood what he was to have. I did, however, make it plain to his wife that he was to have an artificial opening.

DR. CRILE: Did you understand things that way, Mr. S.? Do you remember what you understood at the time of operation?

PATIENT: Yes, sir.

DR. CRILE: Dr. Turnbull, why did you decide in this particular case to do an abdominoperineal resection instead of an anterior resection or a pull-through procedure?

DR. TURNBULL: These cancers were located low in the rectum, and of course for any lesion in the lower rectum, sphincter-saving operations are not applicable because there is no hope for cure. We did the maximal operation for cancer of the rectum.

DR. CRILE: Mr. S., are you satisfied now? You were very much opposed before operation; you thought it would be a terrible thing to have a colostomy. What is your feeling about that now?

PATIENT: It's all right now.

DR. TURNBULL: In the postoperative period Mr. S. was so upset that for 4 or 5 days he would neither eat nor drink, and it was difficult even to talk with him. I don't know who here would not be upset in such a circumstance. But after he went home, his wife, who is very courageous, did a lot to help him understand his problem. When he found that his health was coming back, he accepted the colostomy.

DR. CRILE: Mr. S., do you have any difficulty with it—any accidents or embarrassing situations?

PATIENT: No, not once.

DR. TURNBULL: How do you care for the colostomy? How often do you irrigate it?

PATIENT: Every other day.

DR. TURNBULL: Does that take you about an hour?

PATIENT: Forty-five minutes.

DR. TURNBULL: About the average time. You are able to carry on your work operating a Diesel engine?

PATIENT: Yes, sir.

DR. TURNBULL: Are you socially active?

PATIENT: Yes.

DR. TURNBULL: There was a period after operation when Mr. S. was afraid to carry on his old activities. Now he is active, and he says he can eat anything. Although in the early months the colostomy is very sensitive, sooner or later most of these persons can eat almost what they want to. Thank you very much, Mr. S.

DR. CRILE: The next patient had an entirely different type of lesion, although I should like to emphasize that it was at approximately the same level. The lesion itself was different and it behaved differently.

DR. TURNBULL: The rectum was very much

FIGURE 1 *(left)*. Multiple carcinomas and polyps. Abdominoperineal resection.

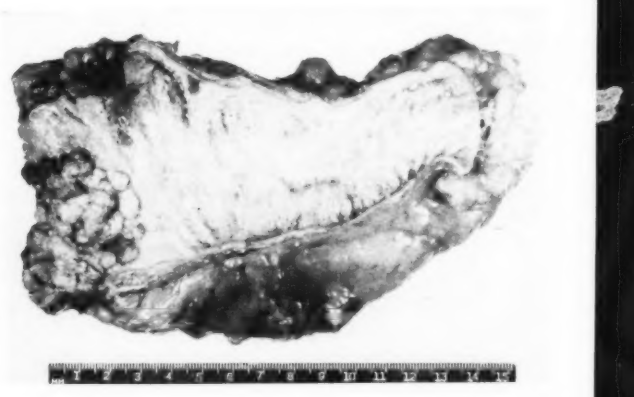

FIGURE 2 *(right)*. Diffuse papillary adenoma of the rectum.

contracted, and coming down toward the anus the tumor appeared to be cut across. There was a diffuse papillary adenoma of the rectum (Figure 2). It engulfed or grew over about two-thirds of the lumen above the dentate line and extended upward.

DR. CRILE: This lesion was basically benign. The removed specimen shows areas in which adenocarcinoma is present on the surface of the lesion. Dr. Turnbull, why didn't you do a combined abdominoperineal resection in this case?

DR. TURNBULL: First we saw a lesion that appeared to be clinically benign. It was soft, but it was growing over too great an area for local treatment. We biopsied it in 20 or 30 places to determine that the carcinoma was *in situ*, not invasive; therefore an operation could be done with preservation of the sphincter. We could operate on this patient as if the neoplasm were benign.

DR. CRILE: Suppose this patient had been studied and a pathologist whom you did not know personally stated that this was an adenocarcinoma. Would you accept that at face value or would you go and talk to that pathologist and review the slides with him before you decided on the operation?

DR. TURNBULL: I would want to establish a close liaison with the pathologist prior to surgery. The pathologist would also ask me, "Does this biopsy represent the entire tumor?" This is equally important. If I weren't satisfied with the report I would re-biopsy the tumor in many places, as we did in this case, to determine whether the biopsy or tissue report was representative of the whole tumor.

DR. CRILE: No one biopsy would tell the story, because there may be one type of tumor in one place and another type in another place. It is essential to get parts of the base, to get multiple representative sections, and to discuss the problem with the pathologist to see whether you are dealing with true invasive carcinoma or with some of the more clinically benign lesions, such as this one. The lesion in this case was removed with a very narrow margin, perhaps not more than 1 or 2 cm. of normal rectal tissue below. Dr. Turnbull, will you describe the operation?

DR. TURNBULL: This is a Hochenegg type of pull-through procedure with preservation of the external sphincter—nothing new at all. Dr. Hochenegg described this operation in about 1886. One proceeds as in an abdominoperineal resection, frees the rectum up, down to the levators from the abdominal side, and with the patient in the lithotomy position a circular incision is made at the dentate line, the finger is inserted in the presacral space, sweeping the levators off the rectum, and the rectum and colon are pulled down through. After the rectum is out, it is cut off. The sigmoid is left projecting through the sphincters, and about a week later this is cut off and stitched to the anal canal skin. That retracts and the patient ends up with only an external muscle, a voluntary muscle.

(To the patient): When I first told you that this was carcinoma in adenoma, you had your mind set against having an artificial opening, did you not?

PATIENT: Yes.

DR. TURNBULL: It was only some time after the tumor was investigated that we decided to do a compromise operation, with preservation of the sphincter, and then you agreed to have surgery.

PATIENT: Yes.

DR. TURNBULL: But you did go home and think about it. I think the term "cancer" was very instrumental in getting her back.

How do you regulate bowel movements?

PATIENT: I have a regular bowel movement once a day.

DR. TURNBULL: Do you slip between times?

PATIENT: No.

DR. TURNBULL: Can you tell when you are going to have a bowel movement?

PATIENT: Yes, I have a slight cramping.

DR. TURNBULL: In the left lower quadrant, the region of the sigmoid. Are you able to tighten up the sphincter and get to the bathroom in time?

PATIENT: Yes.

DR. TURNBULL: Are you careful of your diet, particularly about foods that might cause a loose stool?

PATIENT: Yes.

DR. TURNBULL: She is very satisfied with

this operation, as Mr. S. is with his. Neither patient knows what the other type of operation is for. Most doctors are worried about the sphincters. The patients come to us only to have the tumor removed. Therefore this is much like being married—one chooses a wife and if there is no better woman in one's life one feels that his choice is satisfactory.

DR. CRILE: I think we must admit that each procedure has its advantages and disadvantages, and if a person can have an almost perfect result, which the majority of pull-through patients do, with a sense of control if the operation is performed correctly from a technical point of view, there is no question that it is better than having a colostomy. It would not be better, however, if it meant that any chance of permanent cure was sacrificed. The reason these patients come to us has nothing to do with colostomies or anything else; they come to us for cure of cancer, and that is our first obligation to them. So I emphasize again that in these carefully considered cases we should use selectively one type of operation or another, as Dr. Turnbull did here, knowing that it is perfectly safe in one case to do a pull-through procedure and that in another case it would be folly.

DR. TURNBULL: Very thorough investigations are essential before the final decision is made for these low-lying, benign-appearing lesions.

This next patient came to see us because of mucous colitis of many years' duration, and cramps. The first film represented the colon filled with barium, and it appeared perfectly normal. The second film, the evacuation film, disclosed a large polypoid tumor lying at the rectosigmoid. We want to call attention to the fact that the evacuation film is worth a great deal.

DR. CRILE: How would you handle a tumor like that? What is the first thing you would do?

DR. TURNBULL: First of all, we didn't know whether the tumor was benign or malignant. In this case the lesion was visualized through a large operating scope. The tumor was so large it wouldn't fit into the scope. We biopsied it 20 or 30 times, and it was reported as carcinoma *in situ* in adenoma.

DR. CRILE: Clinically, again, here is the question of interpretation of carcinoma. This tumor was not invasive; it was carcinoma growing *in situ*, amenable perhaps to local treatment. How about taking it out from below?

DR. TURNBULL: It was too large, and one of the principles in removing benign tumors from below is that one must see the base or stalk of that tumor. We didn't know where this tumor was coming from.

Through a low midline incision the rectum was freed and opened transabdominally, and the tumor was found to be on a long twisted pedicle and was removed.

DR. CRILE: This tumor, although perhaps pathologically carcinoma in papillary adenoma, is still clinically benign, and it was handled satisfactorily by local excision with complete preservation of the rectum.

We have other problems quite different from this, and the next case is that of a 38 year old woman who had an early small invasive carcinoma.

FIGURE 3. Carcinoma of upper rectum. Anterior resection of rectum and sigmoid colon with anastomosis.

DR. TURNBULL: Figure 3 shows the surgical specimen. Anterior resection of the sigmoid and upper rectum was done. The carcinoma was very small, about the size of a dime.

DR. CRILE: This patient's only symptom had been slight bleeding from the rectum. X-rays of the sigmoid had shown no abnormalities. I think it is extremely important that we realize that there are several blind spots in the colon, one of them being the flexure of the sigmoid where one loop gets behind the other, and the radiologist may completely miss the lesion unless he makes lateral films; another blind spot is the splenic flexure, where the same thing may occur. So do not rely on the x-ray in lesions of the low sigmoid. *Proctoscopic examination should always preface roentgenologic studies.*

It says in the textbooks that 75 or 80 per cent of these lesions of the colon are palpable by digital examination. What is your feeling about that, Dr. Turnbull? Were you able to feel this one?

DR. TURNBULL: No, we couldn't feel this one. It was located a little too high and was so small that the patient could not push it down by straining.

DR. CRILE: What do you think about the statistics which say that 75 or 80 per cent of these carcinomas of the colon are palpable digitally?

DR. TURNBULL: Many of these tumors are located up at the rectosigmoid and are large enough so that the patient can push them down by straining. Many are in the sigmoid and the sigmoid colon is lying in the rectovesical pouch or the cul-de-sac and therefore the mass can be palpated. This accounts for the 75 to 80 per cent.

DR. CRILE: In other words the most common tumors of the rectum are characteristically located just out of reach of the examining finger, and when the lesion is small the diagnosis cannot be made by rectal examination alone. Those figures which say that 75 to 80 per cent of carcinomas of the colon are palpable refer to advanced carcinoma when it is finally discovered, not to early carcinomas. Carcinomas, of course, should be discovered early.

It is also important to do the rectal examination correctly; you can examine much higher with the patient in the lateral decubitus position than with the feet up in stirrups. But even that is not enough. You must sigmoidoscope these patients to make the diagnosis. Anyone with rectal bleeding or change of bowel habits should be sigmoidoscoped.

Dr. Turnbull, what did you tell this patient preoperatively?

DR. TURNBULL: I told her that the cancer (and I used that word) was at a controversial level—that is, at a level at which any one of several operations could be done.

DR. CRILE: What did you find and do at operation?

FIGURE 4. Carcinoma arising in polyp.

DR. TURNBULL: I made it clear to the patient that I would like to make the decision at the time of operation, not before, and we made no promises. Actually we found this small tumor lying 2 inches above the peritoneal reflection, so there was no danger of lateral spread. Therefore, pull-through or abdominoperineal resection would be equally as radical for the cure of this cancer.

DR. CRILE: Do you feel that the curability of this lesion is perhaps just as great with a pull-through type of procedure because it is high and you can take out just as much of the colon and the mesentery above as you want to, and that unless it is low where it is beginning to spread laterally the pull-through perhaps gives as high a curability rate in this location as does any other operation?

DR. TURNBULL: It certainly does.

DR. CRILE: Why not an anterior resection in this case?

DR. TURNBULL: Her body build was such that it would have been difficult. It could have been done, but I could not have gotten as far below the tumor as I wished.

DR. CRILE: By that we mean resection with end to end anastomosis. This is one of those borderline situations in which any one of these three procedures might be applicable, but I certainly think that an abdominoperineal resection, whether finished by pull-through technic or by colostomy, is curative. These decisions are never made until the end, because the procedures are identical for all three operations right up until the time the bowel is divided.

DR. TURNBULL: We cannot do a small operation for a small cancer. In this case there were 2 lymph nodes involved high in the sigmoid mesentery.

DR. CRILE: You would think that in the case of such a small lesion, some local operation would be all that was necessary, but cancer is cancer and this is frank invasive cancer with lymph nodes involved.

A small ulcerating cancer arising in a benign polyp is seen in Figure 4. The patient in this case was subjected to low anterior resection. The rectum was divided 3 inches below this lesion, with end to end anastomosis. The sigmoid and the mesentery were taken out in radical fashion.

Figure 5 illustrates what looks like a cancer located in the rectum, at 5 inches. It certainly is not; it is benign, but with adenocarcinoma *in situ* again. The tumor was completely coagulated, and 3 months later it had grown to the same size again. This woman's sister died of cancer of the rectum. We felt that biologically this tumor, in spite of being only adenocarcinoma *in situ*, could not be trusted, because it grew too rapidly. We resected the upper rectum and all the sigmoid and made an anastomosis. No lymph nodes were involved, and the lesion was strictly superficial, limited to the mucosa.

FIGURE 5. Papillomatous polyp with carcinoma *in situ*. Upper rectum resected with anastomosis.

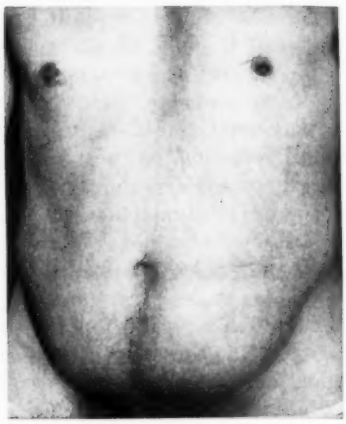

FIGURE 6 *(left)*. Multiple cancers of colon. Subtotal colectomy with ileosigmoid anastomosis.

FIGURE 7 *(right)*. Surgical approach to subtotal colectomy.

What is the significance of polyps in the rectum, Dr. Turnbull? What is the first thing you do after observing polyps?

DR. TURNBULL: The finding of a polyp or multiple polyps in the rectum should make one wary about additional lesions above. We have x-ray and double air contrast studies done in all these patients. We are looking for polyps or cancers above before treating the rectal polyp.

DR. CRILE: Multiple cancers and polyps are seen in Figure 6; operation was done in this case in one stage, and continuity re-established by anastomosing the terminal ileum to the upper rectum.

DR. TURNBULL: Although this man was 68 years of age, the entire colon had to be removed radically. Figure 7 shows the approach, low midline, and off to the costal margin on the left.

DR. CRILE: Speaking of polyps, what about those which occur with ulcerative colitis? For instance, Figure 8 shows the surgical specimen from a case of ulcerative colitis extending around into the cecum; although it wasn't too apparent on the x-ray, ulcerative colitis was definitely present. Polyps were also found. Do you think one is justified in watching these patients with ulcerative colitis which has been present for 10 or 15 years and who show polypoid change, to see whether cancer will develop? How often should they be x-rayed?

DR. TURNBULL: I think it is ridiculous to x-ray these patients and watch for it. Such cancers are deeply ulcerating, and the situation usually is hopeless long before one can be found. In intractable, long-standing cases we think prophylactic removal of the colon is indicated.

DR. CRILE: In other words, you make up your mind either that this is the type of case of intractable ulcerative colitis in which there is statistically such a large chance that cancer will develop that the colon should be removed prophylactically, or that in a patient who has had a satisfactory remission and in whom there is no polypoid change and little danger of cancer it is useless to follow and watch and observe them because the symptoms of cancer and of colitis are the same and the x-ray does not tell you in time to cure it if it is cancer.

We disagree on the management of ulcera-

FIGURE 8. Polyp in ulcerative colitis. Subtotal colectomy.

tive colitis with those who say that early ileostomy should be performed as a preliminary procedure followed by stage operations. For several years we have practiced one stage removal of the colon, sometimes including the rectum, more often doing the ileostomy and the colon around to the low sigmoid as the first stage. What about our results?

DR. TURNBULL: The mortality rate is extremely low, and the patients have short hospital stays and recover promptly. If any active disease is left behind, there is a slow convalescence.

DR. CRILE: We think there is a lower morbidity rate and a lower mortality rate with one stage, and this is particularly true in the severely ill, toxic patient. We believe the mortality rate is definitely lower if the disease is removed at the first operation, because these patients don't die of the operation, but of the disease and its complications.

One problem which comes up frequently is obstruction of the colon. For instance, take the case of a patient who has an obstruction of the colon caused by a lesion in the sigmoid. There is a huge dilated transverse colon and cecum. What is the first thing to do under such circumstances?

DR. TURNBULL: We investigate the patient briefly and find out where the obstruction is. In the case to which you refer, there was an obstructing lesion at the junction of the descending and sigmoid colon.

DR. CRILE: Could you tell whether that was cancer or diverticulitis, or what it was?

DR. TURNBULL: No, we couldn't tell. The x-ray was not typical of either cancer or diverticulitis. A diagnosis was made of an obstructing neoplasm. However, when the colon is so large and thick-walled, one might think that the condition has been present for a long period of time.

DR. CRILE: How do you decompress these?

DR. TURNBULL: I think I would prefer a tube cecostomy. Anything else would be a major operation. This huge transverse colon would have to be delivered through the abdominal wall by means of a large incision. We think cecostomy is the better operation. After the back pressure is relieved, the lesion usually opens up and the colon empties itself. I doubt if one can lavage out a distally obstructed colon.

Myotonia Atrophica

A CLINICOPATHOLOGIC REVIEW WITH REPORT OF 5 CASES

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Five cases of myotonia atrophica are reported, and a clinicopathologic review is presented. All 5 patients were related. The characteristic features of the disease and the treatment methods which have been tried are discussed.

MYOTONIA atrophica is a familial disease of modified mendelian inheritance characterized by myotonia, muscular atrophy of a characteristic pattern, and various combinations of such extramuscular manifestations as gonadal atrophy and insufficiency, cataracts, frontal baldness, electrocardiographic changes and eventual psychic changes.

Although the combination of myotonia and muscle atrophy was described as early as 1888 by Dana, it was not until 1909 that Steinert published a full description of the disease, calling attention to the association of the muscle changes with extramuscular dystrophic features such as premature frontal baldness and gonadal atrophy.[1] From then on, other dystrophic manifestations were recognized one by one until the entire clinical picture of myotonia atrophica developed as it is known today.

The protean manifestations of the disease drew the attention of numerous investigators and produced a wealth of literature about this disorder. Several hundred cases were reported in the English and foreign literature, but the exact incidence of myotonia atrophica is unknown since probably many cases have gone unrecognized. Distribution between the sexes is approximately equal.

R. D. TREVATHAN

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Symptomatology

Myotonia atrophica usually has its onset between the ages of 20 to 30 years.

Myotonia is seen early in the course of the disease, tending to disappear as the muscles atrophy. The myotonia may develop many years before the other manifestations. Therefore, frequently the first symptom is difficulty in releasing objects which have been grasped. This condition is worse after rest and diminishes with each contraction on repetition of movement; it increases with an increase in force of contraction. Myotonia also can be demonstrated by mechanical and electrical

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stimulation of the muscle. If the affected muscle is struck with a percussion hammer, the contraction shows a prolongation of the phase of relaxation. The myotonic contraction is never painful. Myotonia occurs classically in myotonia congenita (Thomsen's disease), and only under the influence of cold in paramyotonia congenita (Eulenburg's disease). In persons with severe myxedema, muscular hypertrophy and myotonia sometimes can be seen. Myotonia is most commonly seen, however, in myotonia atrophica.[2]

Atrophy of the muscles may begin at any time after onset of the illness, and it is therefore not uncommon simultaneously to find myotonia in one group of muscles and atrophy in another. Myotonia may be minimal or already absent at the time the patient is first seen. In some cases there is not even a past history of myotonia. In a typical case of myotonia atrophica there is an expressionless face with drooping mouth. Ptosis of the eyelids occurs late in the disease. The voice is nasal and expressionless. Atrophy of the temporalis, masseter and sternocleidomastoid muscles usually is severe, leading to much difficulty in flexing the neck and legs and giving the appearance of a "swan neck" deformity when the patient is seen in an upright position. Atrophy and loss of strength of muscles of the extremities exceed in severity that of the central musculature. There are no fasciculations, and the "dystrophic" facial movements of facioscapulohumeral muscular dystrophy do not occur. In cases with advanced wasting, the deep reflexes are diminished or even absent. No pathologic reflexes are ever present and no sensory abnormalities are found.

Both men and women tend to develop cataracts, and most cases show some evidence of lenticular opacity to slit lamp examination. In some cases trophic changes of the cornea are found.[3,4] Alopecia may develop at an early age in both sexes. Testicular atrophy and androgenic deficiency are seen in men, who frequently are sterile and sometimes impotent. Women show evidence of ovarian hormone deficiency and may have menstrual disturbances. The asthenic build of these patients is considered rather characteristic.

The heart is frequently involved in myotonia atrophica, the percentage of cases with cardiac abnormalities increasing with the period of duration of the disease. In a group of 98 cases collected by 33 authors in which electrocardiograms were made, 61 showed abnormal tracings. Low P waves and prolonged PR intervals and intraventricular conduction time were the most frequent aberrations. In most cases there was elevation of the ST segment.[5] In addition, such changes were found as bradycardia, auricular flutter, A-V dissociation and bundle-branch block. Blood pressure usually is somewhat low and the pulse is small. The heart is usually normal in size. Heart sounds are normal, but splitting of the first sound in the mitral area may be heard.[6,7] It was pointed out that these abnormal findings could not be attributed to the administration of quinine or to coronary artery disease. It was postulated that the myocardium might be affected by the same process as that affecting the skeletal muscles.[5] In the case of sudden and unexplained death from heart failure of a man who suffered from myotonia atrophica, postmortem examination revealed no cardiac abnormality apart from ventricular dilatation. Unfortunately the A-V bundle was not examined.[7]

Billings and Ravin[8] studied 11 patients from a psychiatric standpoint. No real depression was noted although the patients seemed to be depressed due to slow movements and myopathic facies. There was no elation, but some pseudo-optimism was a characteristic feature. The urge and drive in these patients appeared to be unchanged; however, the physical capacity was lacking. Withdrawal, when it occurs, is not a personality compensatory mechanism but it is forced on patients by the physical handicaps. This study revealed no prevailing type of personality organization or temperament common to patients with myotonia atrophica. Intellectually, most patients were poorly endowed. No correlation, however, could be made between the intellectual deterioration and the severity or duration of the disease. No particular psychopathologic process was evident in this group.[8]

Radiologic Findings

Caughey reported on 13 patients with myotonia atrophica, all of whom revealed some radiologic abnormality of the skull. The most common findings were small to very small pituitary fossae. Thickening of the calvaria was seen in 9 cases. Hyperostosis frontalis and hyperostosis parietalis were seen in 9 cases and were pronounced in 3. Enlarged sinuses were noted in 8 and an elongated mandible was seen in 2.[1] In Rougues' 4 cases, the calvaria was distinctly thickened in 3. Large frontal sinuses were found in 2, small pituitary fossae in 2 and small pituitary fossae bridged over by calcification in 2.[9]

Laboratory Findings

The clinical laboratory is of very little help in the diagnosis of myotonia atrophica because the abnormalities found by means of laboratory tests are neither constant, pronounced nor specific.

A low basal metabolic rate is a frequent but not constant finding. Uniformly low urinary 17-ketosteroid excretion was found in 9 cases of dystrophia myotonica in which endocrine studies were done. Five of these patients showed increased follicle-stimulating hormone excretion.[10]

Although a low blood sugar is commonly described, on a well controlled study no statistically significant difference from normal was found in the glucose tolerance test or the metabolism of sugar in dystrophia myotonica.[11]

Slight to moderate creatinuria observed in 3 cases studied was neither so constant nor so striking as is seen in progressive muscular dystrophy; it was also less strongly affected by the administration of glycine than in the latter disease. The decreased urinary output of creatinine is also a disputed finding.[12]

Serum potassium levels were studied in a group of 11 cases. Patients who had marked myotonia but only slight atrophy showed a very definite fall in serum potassium after exercise. Patients who had slight myotonia but definite wasting showed no alteration in the potassium level after exercise, but many of them showed a low resting level.[13]

Pathology

The histopathologic findings from several autopsy reports are confined to the endocrine glands, central nervous system and the voluntary muscles.[14-17]

The most constant anomaly of the endocrine system was atrophy of the testicles. The hypophysial findings ranged from no changes to some alterations in the chromatophil cells of the anterior lobe—mostly increased size of the basophilic cells.

No histopathologic changes were found in the spinal cord, sympathetic chain or peripheral nerves, according to one investigator. Even special fiber analysis of the dorsal and ventral roots did not reveal any pathologic process.[17] Another author found moderate secondary retrograde changes in the motor ganglion cells of the anterior horns of the cord and especially in the facial nucleus.[15]

The most uniform findings were the histopathologic changes in the muscles in biopsy and autopsy materials. An inward migration of nuclei from the periphery of the muscle fibers to the center was seen, with the formation of long nuclear chains. The myofibrillae are often destroyed without a corresponding decrease in the sarcoplasm content. These changes, however, are not considered specific or pathognomonic. They are similar to those seen in myotonia congenita and also in congenital paramyoclonus, and differ from those seen in inflammatory and degenerative myopathies such as progressive muscular atrophy, progressive muscular dystrophy and myasthenia gravis. They are evidently the result of wear and tear, being the effect and not the cause of the clinical manifestations.[18,19]

Pathomechanism

Myotonia atrophica is now considered a definite disease entity, with its pathomechanism not well understood. It is agreed, however, that the cause is not in the muscles, the peripheral nerves or the central nervous system. It is probably a metabolic disorder, producing abnormal muscular contractions that ultimately bring on the pathologic changes of atrophy. The extramuscular dystrophies such

as baldness, cataract, gonadal atrophy, etc., are probably the expressions of this metabolic disturbance.

A disturbed acetylcholine metabolism at the myoneural junction may play an essential role in the pathomechanism of this disease. Minz studied acetylcholine and cholinesterase content of the myotonic and nonafflicted muscles of the same patient. He found a reversed ratio between acetylcholine and cholinesterase in the myotonic muscles, with the cholinesterase being markedly diminished when compared with the ratio in the normal muscles.[20]

The increased acetylcholine activity (increased production or decreased destruction by cholinesterase) is an accepted explanation of the pathomechanism in myotonia congenita. If one would also accept the suggestion that myotonia congenita and dystrophia myotonica were identical, the former being merely an early stage of the latter, the understanding of dystrophia myotonica would be simplified. The issue, however, is still very controversial, being supported and opposed by about an equal number of authorities in this field.[21]

Treatment

In spite of numerous therapeutic experiments, no effective treatment has been found so far for this disease.

Quinine was found to be effective in controlling myotonia in the muscle groups so affected.[22] Testosterone brought improvement in 2 male patients with testicular atrophy by increasing muscle strength and the feeling of well being and by lessening fatigability. Temporary withdrawal of the drug was accompanied by decreased dynamometric values.[23] In one case some improvement was observed following the administration of vitamin E.[24] Two patients were treated with ACTH with some subjective improvement, but there was no objective evidence of increased muscular function.[25] Cortisone was given in 2 cases, with the abolishment of the myotonia but no other benefit to the patients.[26]

Case Reports

Case 1—A 33 year old married white man was admitted to the hospital on March 20, 1951, complaining of muscular weakness and easy fatigue. These difficulties had their onset in 1945, prior to which time he had considered himself well and strong. He then noted the insidious onset of weakness in the grip of the hands, and difficulty in releasing objects once they had been grasped. These symptoms gradually became more marked, but were not severe at the time of his discharge from military service in 1945. Since that time there had been a slow but inexorable progression of weakness of the arms and hands, and the patient became unable completely to flex the fingers, feet or toes. There was progressive weight loss, totaling approximately 25 pounds. At the time of admission he complained of dyspnea after mild exertion, associated with a sense of constriction in the precordial region. No edema was noted. He denied having any sensory disturbance, change in libido, or loss of sphincter control or of visual acuity. He also denied any family history of conditions similar to his own, but this latter statement subsequently was found to be false. This patient is the father of four children.

The patient was 72 inches tall and weighed 133 pounds. The scalp was covered with thick, dark hair. Routine eye examination revealed no evidence of cataract. Speech was of a nasal quality. The intellectual level appeared to be normal. The face was expressionless except for fleeting smiles. The patient walked with a steppage gait, lifting the feet high to avoid dragging the toes. Cranial nerves were intact. There was atrophy of the sternomastoid, masseter and temporalis muscles and of the muscles of the extremities, with pronounced bilateral weakness of the hand grip, flexion and extension of the wrists and of the feet and toes. The deep reflexes showed marked diminution. No pathologic reflexes could be obtained and no fasciculations were seen. Sensory changes were absent. The testicles were normal.

Muscle-nerve tests showed definite partial reaction of degeneration. Routine laboratory tests gave normal results. Electrocardiograms showed auricular fibrillation. The electroencephalographic tracing revealed no abnormal-

ity. Biopsy of the left gastrocnemius muscle showed normal striation.

Case 2—A 30 year old unemployed man, a brother of the patient in Case 1, was admitted to the hospital on April 6, 1952, with a respiratory infection. He had considered himself quite healthy when he entered military service in 1942. Physical examination on induction revealed atrophy of the right testicle of undetermined cause. He had mumps without orchitis while stationed in the United States. Later he was sent overseas and was hospitalized because of trench foot. During this hospitalization he noticed the gradual onset of weakness of the forearms without myotonia. During this and several subsequent military hospitalizations he was studied by several neurologists who were unable to make a diagnosis of neurologic disease. After discharge from military service he worked as a farmer until 1948, when he had to stop work because of steady progression of his weakness, which had become generalized. He described some loss of sexual prowess for over a year prior to the present hospital admission. He had been married for six years, but there were no children. He described a weight loss of 40 pounds during a five year period.

The patient was 72 inches tall and weighed 140 pounds. He had an expressionless face, a droopy mouth and a muffled voice with a pronounced nasal quality. Frontotemporal

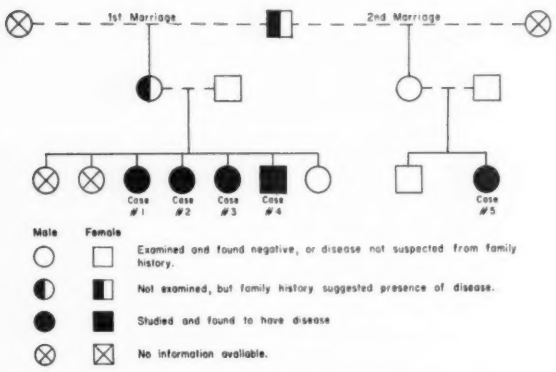

FIGURE 1. Occurrence and distribution of myotonia atrophica in the family of our 5 cases.

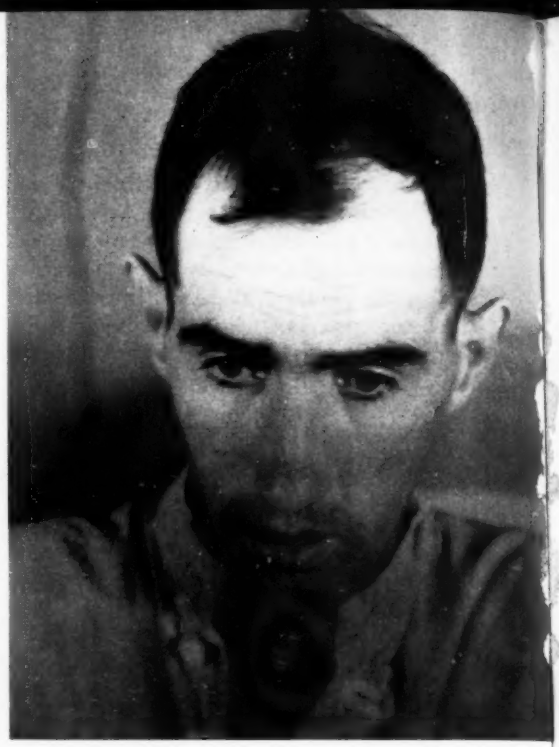

FIGURE 2. Characteristic expressionless face with droopy mouth, a diagnostic feature of myotonia atrophica.

baldness was present. Mental status appeared normal. There was a very high, narrowly arched palate. Routine eye examination revealed no evidence of cataract. Both testicles were atrophic, this being particularly marked on the left. The cranial nerves were intact. There was pronounced atrophy of the temporalis, masseter and sternomastoid muscles and the muscles of the extremities. Muscular weakness was marked, particularly in the extremities. No fasciculations were noted. The patient walked with a steppage gait. There was no sensory disturbance or pyramidal tract involvement. Deep reflexes were hypoactive.

Routine laboratory tests were normal. Protein-bound iodine was 5.7 mg. per cent. The chest x-ray on admission showed infiltration in the cardiohepatic angle, but this subsequently cleared. Skull x-rays were negative. Electrocardiogram revealed a prolonged PR conduction time (0.12 second) and high ST segments in some leads.

The patient was treated with thyroid extract, later with cortisone (100 mg. daily for five days; then 200 mg. daily for three days),

and then with ANTUITRIN S® (1000 units three times weekly) without demonstrable benefit. A short course with ACTH (100 mg. daily for six days) similarly failed to produce even subjective improvement.

He was readmitted on July 30, 1952, complaining of irregular heart action of two days' duration. Electrocardiogram showed a 3:1 auricular flutter. This was converted to regular sinus rhythm with digitalis after quinidine and PRONESTYL® failed.

Case 3—A 26 year old housewife, sister of the patients already described, was interviewed at her home in a remote rural district under circumstances which precluded any complete physical examination. She denied any history of weakness, myotonia or visual defect; however, she showed unmistakable evidences of myotonia atrophica. She had a high, arched palate, and there was a slight nasal quality to her speech. There was definite atrophy of the masseter, temporalis and sternomastoid muscles and of the muscles of the forearms and calves. Grasp of the hands was weak and there was definite myotonia. A mild steppage gait was seen. The patient was married and had two children.

Case 4—The oldest brother of the patients already described (38 years old) was interviewed under the same conditions as his sister. He denied any knowledge of his illness, attributing his crippled condition to residuals of an automobile accident. He had a muffled voice and a high, arched palate, but there was no evidence of cataract or defective vision. There was ptosis of the eyelids, and profound weakness and atrophy of the masseter, temporalis and sternomastoid muscles and of the muscles of the extremities. No myotonia was present. There was a marked steppage gait. This patient was divorced; there had been no children.

Case 5—An unemployed white man, 55 years of age, a second cousin of the 4 patients described, was admitted to the hospital on November 14, 1951, with generalized muscular weakness of many years' duration. The weakness had its onset around 1925, presenting symptoms of weakness of the hands and difficulty in relaxing the grip. The weakness spread slowly and relentlessly to involve all muscles of the extremities. Frontoparietal baldness developed at the age of 30. The voice was never involved. After onset of disability the patient was able to do only light work, and he had been totally incapacitated for the past nine years. He had had no fasciculations, pain, visual difficulty, sensory disturbance or sphincter weakness and he denied any loss of libido. He described a weight loss of about 25 pounds in 25 years.

On physical examination the patient appeared chronically ill; he was 71 inches tall and weighed 133 pounds. Mental status was grossly normal. Advanced frontotemporal baldness was noted. Ptosis of the eyelids was present, as well as prominent arcus senilis. There was no sign of cataract formation. The testes were atrophic. There was atrophy of the temporalis, masseter and sternomastoid muscles and of the muscles of the extremities. Muscular weakness was far advanced. He could not flex the forearms or hold out his arms against the pull of gravity. He required aid to get into an upright position, but once there could walk with a marked steppage gait. Speech was not definitely affected but was difficult to judge because he was edentulous. Deep reflexes were hypoactive, and toe reflexes normal. No sensory changes could be demonstrated. This patient spent all his time in a wheel chair except for exercise periods under care of the corrective therapists.

Results of routine laboratory tests were within normal limits. The glucose tolerance test gave a flat curve with a fasting level of 90 mg. per cent and a high of 122 mg. per cent. Electrocardiogram showed bradycardia, inverted T waves in leads 1, V5 and V6, and a deep Q with high ST segment in lead 3. Skull x-rays were negative. The patient was treated with testosterone (25 mg. daily for seven days; then twice weekly for five weeks and weekly for three months) and later with cortisone (100 mg. daily for five days and 50 mg. daily for four days) without benefit.

Discussion

The hereditary nature of myotonia atrophica and its distribution in the family of our

patients is illustrated in Figure 1. The common ancestor of our patients was found to be the paternal grandmother. She had bilateral cataract operations about 15 years before her death at the age of 74, but no other evidence of dystrophia could be elicited. She was the grandmother of the patient in Case 5, from her second marriage. From the first marriage came the father of the other 4 patients studied. He died at the age of 60 following years of "invalidism." It is suspected that he had the disease.

The two brothers (Cases 1 and 2) and their second cousin (Case 5) were studied in the hospital. Two siblings (Cases 3 and 4) were seen in their home and therefore were not subjected to a detailed examination. There was, however, no doubt about the diagnosis of myotonia atrophica in either of these 2 cases. The atrophy of the muscles in typical distribution, the nasal speech, together with a family history, were enough to make such a diagnosis. The diagnosis was unmistakable, of course, in the other 3 patients, who were studied in the hospital.

It was interesting to observe that none of these patients were concerned about their physical condition; some did not even consider themselves sick. From available information, the correct diagnosis had never been made before in any of the 5 cases. Myotonia was present in the early stage of the illness in Cases 1 and 5. It was found by us in Case 3.

Asthenic body build was noted in 4 of the 5 cases. Definite electrocardiographic abnormalities were found in all 3 patients in whom this examination was made. Testicular atrophy and baldness were present in 2 of the 4 male patients. Slit lamp examination of the eyes was not carried out for technical reasons. The patients in Cases 2, 3 and 4 had high, narrowly arched palates, so far not described in this illness. X-ray of the skull in 2 cases did not show any abnormalities. We have found that the facial expression of the patients was the most characteristic diagnostic feature. Note in Figure 2 the expressionless face with the droopy mouth.

If one keeps in mind the tetralogy of myotonia, muscle atrophy, the extramuscular dystrophies (cataract, testicular atrophy, baldness, etc.) and familial occurrence, the diagnosis of myotonia atrophica can hardly be missed. Although no effective treatment is known today for this malady, the correct diagnosis will help to plan for the future of these unfortunate patients.

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Surgical Treatment of Diverticulitis

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In many cases of diverticulitis medical management has much to offer. If surgical treatment is chosen, colostomy only is performed at the first stage if there is any question about the operability of the lesion. After a suitable interval resection is done in all cases in which it seems feasible.

A DESCRIPTION of two illustrative cases will, I think, be the best way to present the subject to you. We are very much indebted to the local Cleveland Committee (of the Interstate Postgraduate Assembly) for obtaining this excellent clinical material for us.

EDWARD S. JUDD, JR.

The first case not only illustrates some of the most essential factors of the problem of diverticulitis, but it goes much further than that and brings up an extremely unusual result and one by which we are somewhat baffled.

The patient had a very typical history. Early in 1952 there was a large inflammatory mass in the left side of the abdomen which particularly interested the surgeons and gynecologists. The diagnostic measures were those we all use, and the diagnosis was correct in every respect. I would agree completely with the diagnosis and treatment—namely, a diagnosis of diverticulitis was evident and operation was carried out in stages. I will stress that repeatedly. A loop type of transverse colostomy was done first. Following this, at a suitable interval, the offending area in the sigmoid was resected and an end to end anastomosis was possible.

The patient then returned to her home. After a suitable interval she came back for colostomy closure. She was entirely well for a relatively short period of time thereafter.

She returned to the doctor because there seemed to be a recurrence of inflammatory disease in the left side of the abdomen. This was treated, and correctly, I believe, with antibiotics and conservative measures. She returned to her home only to come back just recently with what I think is an extremely unusual phenomenon, namely, the passage of gas and stool once again through the urinary tract.

She then underwent the only type of operation which would have any effect—another transverse colostomy. Our chief reason for having her here is to demonstrate the type of colostomy that was performed.

You will recall that at the first colostomy a loop was brought up and exteriorized, as we always do. At this time it was realized that an extreme problem existed and that something more diversionary in nature was indicated.

There is complete division of the transverse colon with absolutely no chance for spill-over of the contents into the distal loop. The pa-

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tient states that since the last operation there has been no passing of gas and stool with the urine.

The point now is, of course, that we have here a patient who received exactly the right therapy in an extreme disease. The case perhaps illustrates a recurrence of the phenomenon following the best treatment we have to offer. This is a very important type of case, because in our experience it has been almost unheard of to have a recurrence of the disease process following definitive resection of the offending area of the bowel. The patient here, of course, has some choice in her future management. There is nothing malignant in her case and time is not of the essence. She will decide first of all whether to undergo further surgical treatment and then the decision as to time will be made. At present she is well pleased to be rid of the extremely distressing disease process she formerly had.

Our second patient represents a great problem in diagnosis, one which faces all of you from time to time. I will hasten to state that the diagnosis has not yet been reached. The problem is that of bleeding from the gastrointestinal tract.

Briefly, the patient is 68 years of age. He came to the hospital because of several nonrelated symptoms, but during his examination it was discovered that there was a persistently positive guaiac test for blood in the stool. He was found to have an indirect inguinal hernia and a basal cell epithelioma of the nose, but aside from that there wasn't a great deal in the way of positive findings that was helpful.

He underwent a very thorough examination. The findings so far have revealed a diverticulum of the duodenum. It has been suggested that he might have Meckel's diverticulum. It is very difficult, of course, as you all know, to prove whether Meckel's diverticulum exists. Occasionally we are fortunate enough to get the barium to run into the Meckel's diverticulum and then the proof is very easy, but usually it is a question of suspecting the presence of Meckel's diverticulum and then exploring surgically.

When there is gastric mucosa in the tip of the diverticulum, the same peptic ulcerations can be present as may occur in the stomach, and we must not for one moment dismiss from our thought the possibility of Meckel's diverticulum.

It has been suggested that the patient might have diverticulosis. The question arises: "Of what importance is that when there is blood in the stool?" Some of you may think it is of no importance, but it might be of considerable importance. Diverticulosis by itself does not mean a great deal. A fair segment of our population today has diverticulosis, perhaps without knowing it. It is when the diverticula become markedly inflamed that difficulty arises.

Before we dismiss this man we must keep in mind our old "friend" duodenal ulcer. Occasionally our roentgenologists are led to make a diagnosis of duodenal diverticulum when a duodenal ulcer actually exists. Pseudodiverticulum is not at all uncommon, but we know in this case that the lesion is a true diverticulum of the duodenum.

I do not for a moment believe we would ascribe the bleeding to the duodenal diverticulum.

Many people have diverticula of the duodenum without knowing it. Such diverticula are difficult to demonstrate, of course. We do not expose them surgically very often because not too often can we incriminate the diverticulum as far as the symptoms are concerned.

Meckel's diverticulum will be kept in mind for this man. We do know that hemorrhagic diverticulitis might be a definite possibility. However, he has had no diverticulitis; sigmoidoscopy has been performed and no diverticula were seen, but that does not rule out the possibility of diverticulosis, of course. Perhaps his solution will be a surgical one. At the moment, since he has had his hernia repaired and has had treatment for his basal cell epithelioma of the nose, the blood has disappeared from his stool, so that he still remains a diagnostic problem. Perhaps he is well on the way to complete recovery and may never know.

To go on to a little discussion of surgical management of diverticulitis, I must hasten to state that in the face of the tremendous

strides that have been made in intestinal surgery throughout the civilized world today we still must keep in mind that the treatment of diverticulitis from the surgeon's standpoint may actually be an old-fashioned and perhaps a much better way; in other words, the one stage radical operations that so many surgeons are doing now for carcinoma in the same area of the colon may not be applicable at all for diverticulitis. The extreme inflammatory change that is present may render the operation entirely impossible. Therefore, we feel that there is plenty of room for the good old-fashioned multiple stage operation when we are called to treat these people surgically.

Having considered the matter, what are the indications for surgical treatment of diverticulitis? There are not very many, actually, and we as surgeons must be the first to admit that medical management has a great deal to offer. By no means would we suggest surgical treatment for all cases of diverticulitis. The conservative plan still has a good deal to hold out for these unfortunate individuals. *Perforation*, of course, is one of the greatest complications to harass the surgeon and the medical man alike. There may be a free perforation in which the patient turns out to be a desperately sick individual; more commonly, as in the first case discussed, a large mass surrounds the sigmoid leading to abscess formation and ultimately to fistula formation.

We commonly see *obstruction* in diverticulitis. It may demand immediate surgical intervention. Frequently we tide the patient over in a conservative way, but when we do see diverticulitis producing enough obstruction to cause us to recommend a surgical operation, we usually do a preliminary transverse colostomy first, with definitive resection reserved for later on.

Third is *confusion with cancer*. This is extremely important. The better the roentgenologist, I believe, the more willing he will be to admit that he does not have any final criteria to be certain in every case that carcinoma does not exist. Of course, the two lesions may coexist, but the alert surgeon, cooperating with the alert roentgenologist, will admit that the lesion may be carcinoma and that will lead us into much earlier surgical intervention than if we could be sure in every case that the condition was only diverticulitis.

A more modern step, perhaps, is the consideration of the patient who comes to the office because he has had recurrent bouts of diverticulitis treated conservatively. Perhaps at the time of our original examination he is the picture of health. We wonder what we should do, how far we should go in trying to render him completely certain that he will never have further attacks. He may be getting ready for a foreign trip or taking part in a political campaign and he doesn't want to be tied down in a hospital; he knows the terrible complications that have happened to other people that he has heard about. Is there something that we can do? Yes, we think there is. I will comment on it a bit later. We think that we can prepare some of these people thoroughly with the agents available to us today to carry out a primary, definitive, one stage operation and shorten his process from perhaps a year away from his job to only two or three weeks.

Having decided that an operation is indicated, what operations are available to the surgeon? First I will mention—and probably only to condemn it—the simple suture of a perforated diverticulum. That does find its way into some of the textbooks, but usually the case that we see in surgical consultation reveals not by any means a single isolated sac; there is a large inflammatory mass throughout the left side of the abdomen and the mere finding of and suturing of a perforated single diverticulum seems highly theoretical. Even if it were possible, it seems to be poor surgical practice. We would not expect it to heal. We think something more should be done.

How about exteriorizing the lesion, if it is such an inflammatory affair and a primary one stage operation is not feasible? Yes, that has a place here in an occasional case. The old-fashioned Mikulicz operation is still a good one to keep in mind, lifting the mass out on the abdominal wall and cutting it off perhaps 10 days later. Dr. Fred Rankin introduced to us an idea some years ago which was

very helpful in this problem, namely, his "obstructive type" of resection. In this type of operation the mass may be resected immediately at the first operation and the ends of the sigmoid supported upon the abdominal wall by means of Dr. Rankin's three-bladed clamp (a very nice operation in the occasional case). However, by far the commonest operation at the first stage will be the preliminary colostomy, and I will urge you to keep in mind that we agree 100 per cent with Dr. Simeone and his staff here in performing a *transverse* colostomy. One might be led to try to avoid the watery type of stool which might irritate the abdominal wall if placed too close to the right side, and place the colostomy in the sigmoid colon. For reasons that we will go into a little bit later, we would rather not do that.

An analysis of a fairly large (and we think significant) series of cases—a little more than 200 in all—shows that, in spite of the fact that the diverticulum may be located at any point in the large intestine, for practical purposes almost 100 per cent of the ones that become involved in diverticulitis are located in one little area in the sigmoid. We don't know just why that should be but it is consistent with other series that I know of. Perhaps the rather narrow caliber of the bowel at that point and the more solid character of the stool going through it may have a good deal to do with it, but we know from our own experience and the experience of others that if we are looking for the portion of bowel most likely to be the seat of diverticulitis, that is where it will be.

When we expose the lesion we often find that not only is the bladder threatened, but also the uterus, ovaries, ureters, iliac vessels, small bowel and many other organs may be threatened, and we will be hard put to decide sometimes just how radical an operation we can perform.

FIGURE 1. Diverticulitis of sigmoid with complete obstruction to retrograde flow of barium.

FIGURE 2. Diverticulitis with sigmoidovesicocutaneous fistula (lateral view).

The roentgenogram in Figure 1 was made in the case of a rather fat patient (for some reason many of them are fat). The roentgenologist was alert and did not put in very much barium, but he reported there was an obstruction in the sigmoid and he stopped his examination immediately. We exposed this area surgically and we thought possibly the lesion was carcinoma, possibly diverticulitis. We could not get it out because of inflammatory change, and we did a transverse colostomy well up on the right side. We did not wait our customary six months' interval between stages, but rather explored here in about eight weeks. Fortunately then the lesion was quite easily operable and we were able to remove it, do an anastomosis and at a later stage close the colostomy.

Figure 2 might well be a roentgenogram from the first patient presented. It is a lateral view. The patient happened to be a man in this case—perhaps more prone to involvement of the bladder because no uterus is in the way. The lateral view shows a postoperative situation. The abdomen had been explored previously elsewhere and the fistula which led to the skin followed that exploration; the bladder was also involved in the fistulous process. All we have done for this man is a transverse colostomy placed well up on the right side. He has now returned to his home to convalesce and we hope that within six months there will be enough subsidence of his inflammatory process to allow us to close the bladder in an orderly fashion and resect the diseased portion, again closing the colostomy at a much later time.

Figure 3 illustrates a case in which we thought we were putting one over on the roentgenologist. He made an unequivocal diagnosis of obstructing carcinoma of the sigmoid (Figure 3a). We prepared the patient as well

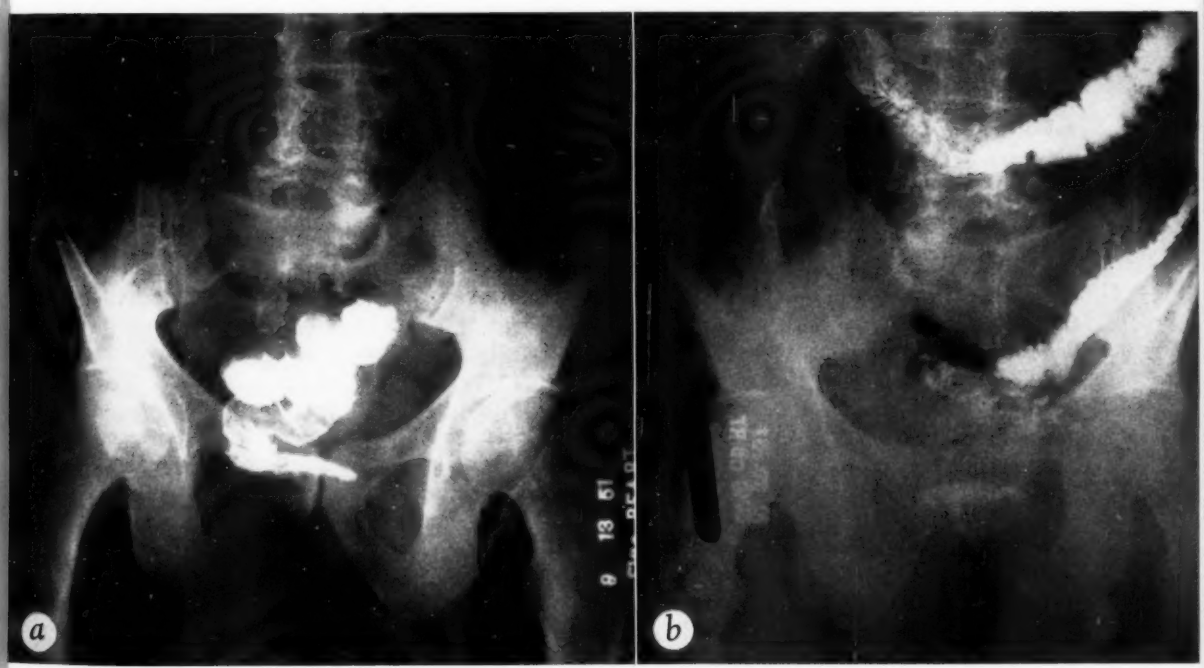

FIGURE 3a. Complete obstruction to retrograde flow of barium which roentgenologist considered to be carcinoma of sigmoid. b. Same patient one month after transverse colostomy. Roentgenologist changes diagnosis to diverticulitis.

FIGURE 4. Improper colostomy for diverticulitis. Stoma has been placed in sigmoid, rendering it difficult for later resection. Arrow points to perforating diverticulum.

as we could and exposed the lesion surgically. We thought when the abdomen was opened that the lesion was a typical diverticulitis because of all the changes we have come to associate with it. However, we couldn't get it out. We did a transverse colostomy. Figure 3b is another roentgenogram of the colon (taken four weeks later) done via the distal loop. We had been able to clear the bowel out very nicely, and the inflammatory change had subsided enough, so now the roentgenologist agreed with us that it was typical diverticulitis with no sign of carcinoma. That gave us a good deal of backing. We waited another five months. We were able to resect the lesion quite well and do an end to end anastomosis and the condition was diverticulitis. The patient has recently been back for closure and has returned to normal activity.

I have included Figure 4 merely to demonstrate a point which I have touched on briefly and which I would like to elaborate a little. This patient came in with a colostomy already made, and we think made in a very difficult position, namely, the low sigmoid. True, the patient had presented to his local doctor quite a problem of an emergency nature; there was severe obstruction, and the doctor did a colostomy, rather properly so, we think. He characterized the mass as a very inflammatory one, but one that he thought was perhaps carcinoma. The patient has a sigmoid colostomy, which certainly diverts the fecal stream nicely and we can prepare the bowel for definitive resection. However, the colostomy binds the entire left colon deep within the abdomen, so when we come to resection it is most difficult to get the bowel properly mobilized. We make a plea, if one is doing colostomy as a preliminary step, to place it in the transverse colon, even off to the right side, if necessary.

A situation—of the type which a gynecologist could get into—involved a diagnosis of a lesion of the left ovary or possibly a tube. There was difficulty in the ovary and tube—they were included in the surgical specimen—but actually the lesion was diverticulitis. The surgeon who is going to be attacking these problems should be prepared to do either type of operation so that several weeks or months later the patient need not be submitted to other types of operation.

A little earlier I alluded to hemorrhagic diverticulitis. Eight per cent of a large series of patients have bled significantly enough to bring them to the doctor for that one reason.

We think there might be bleeding from the gastrointestinal tract in the second patient discussed—no diverticulitis proved, but multiple diverticula seen. In a case handled by my colleague, Dr. John Waugh, he resected most of the colon because there was some question as to just where the bleeding was coming from. The lesion was diverticulosis without diver-

ticulitis. He told me he also found a large Meckel's diverticulum which he removed. Which lesion was doing the bleeding we don't yet know. It has been three or four years and there has been no bleeding since, so apparently the patient was cured.

Still another patient represented a very "rare bird" in my experience. The course of this patient had been followed by the proctologist, who thought there was a polyp of the rectosigmoid and who had been fulgurating this. It was a case of an inverted diverticulum. The patient came to operation rather promptly because he got extremely sick following a fulguration. As far as I know it is the only such case in our file.

What is the best surgical plan when one has decided on surgical treatment? We think that early exploration is the answer if we are definitely certain that it is a case that surgical treatment will benefit. However, we must admit that there are certain cases in which conservative management will play a very definite part.

If we treat the people surgically, we do a colostomy *only* at the first stage if there is any question at all about the operability of the lesion. Unnecessary sacrifice of the bladder or portions of it, of a ureter including a kidney, or the iliac vessels or great lengths of small bowel does not seem a warranted procedure for a benign disease if we can take the easier way out, the long term way perhaps, of colostomy first, followed later on by a much easier and more orderly resection.

After a suitable interval (after colostomy has been established), perform resection in all of the cases in which it seems feasible. It is quite a temptation, after colostomy has been established and the patient responds so beautifully, simply to close the colostomy some months later. We know that we can get away with it. However, as Dr. Cattell remarked in his excellent talk,* "We aren't in the business to be getting away with things; what we are trying to do is to do the best we possibly can for all of the people that we possibly can." From a very large series of cases we have learned that two-thirds of the persons who have colostomies for diverticulitis, without resection, and then the colostomy simply closed later on, get into serious trouble later with diverticulitis in a recurrent form. In other words, one-third of them could get away with it but we don't know in which group our patients might fall. Therefore, if they are in reasonable condition, if there are not some other conditions which would contraindicate it, we insist on resecting the diseased portion, which would be the sigmoid in almost 100 per cent of the cases.We know that after the colostomy has been present for perhaps one year or two years or longer, there may be so much "quieting down" of the disease process that we could get away with closing the colostomy without resection. By and large we resect the diseased tissue first and then close the colostomy as an entirely separate stage later.

To conclude, then, with a footnote for the future, what about some of these people who have recurrent diverticulitis treated medically and conservatively with good results, laying them up for one or two to many weeks in a hospital, then some weeks or months later having the same thing all over again? When they come in just for their annual checkups or to see what there is new in diverticulitis, might we not prepare them thoroughly in the way we would prepare any intestinal lesion for adequate resection, and put them through a one stage resection with immediate end to end anastomosis and get rid of this distressing problem permanently?

We think we are resecting a few more of these than we previously were. We are emboldened now, with the help that we have from our bacteriologic confreres and our internal medicine colleagues, and we are very quick to adopt the advances that they have made, especially in the chemotherapy field. We think the risk has been brought down now to a point where we will consider performing resection in more of these cases as a purely elective measure.

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Surgical Treatment of Hydatid Cyst of the Liver

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A surgical procedure for the treatment of hydatid cyst of the liver is reported. The cyst is formalinized, widely opened and evacuated. The redundant parts of the cyst wall are resected. Omentum is sewn into the remaining liver cavity. Four patients treated by this method were discharged from the hospital 8 to 12 days after operation in good condition.

ZVI NEUMAN

THE surgical treatment of hydatid cyst of the liver in recent years has followed 2 methods. In the first the cyst is marsupialized and drained. With this procedure morbidity is high and prolonged. Patients must remain hospitalized for weeks and months while the abdominal wound continues to drain. In the second the hepatic cyst is evacuated and then closed. This procedure may result in a collection of fluid in the closed cyst and in secondary infection.

In this report is presented a surgical technic for the treatment of hydatid cyst of the liver which has been borrowed from the surgery of hydatid cyst of the lungs. The method has been modified for conditions in the liver parenchyma. In the surgical treatment of pulmonary hydatid cysts, the cyst is first injected with formalin 10 per cent, aspirated, evacuated and finally reduced by intracystic sutures.[1-3] The cyst is not fixed to the thoracic wall nor is it drained.

The technic outlined below, with some modifications, has been used in 4 cases of hydatid cyst of the liver:

1. Right abdominal subcostal incision.
2. Isolation of cyst walls by moist packs.
3. Aspiration, by syringe, of 20 cc. of hydatid fluid. This is replaced by 20 cc. of formalin 10 per cent which is kept in the cyst for 10 minutes.
4. Hydatid fluid is aspirated, and the cyst is widely opened. Spilling of hydatid fluid into the peritoneal cavity should be avoided.
5. Removal of the fixed and shrunken parasitic cyst wall, which has been loosened by the formalin from the adventitious fibrous capsule.
6. Resection of the redundant parts of the adventitious fibrous capsule, to the level of the liver. A knife or cautery is used as indicated by the amount of bleeding. Liver parenchyma should remain untouched.
7. Omentum is sutured into the remaining liver cavity.
8. Closure of abdomen without drainage.

In the 4 cases in which this technic has

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been applied, there have been excellent results. Two patients were discharged from the hospital 8 days after operation in good condition and 2 patients 12 days after operation, also in good condition. These patients have been followed for 6 to 30 months, and are all well at present (Table 1).

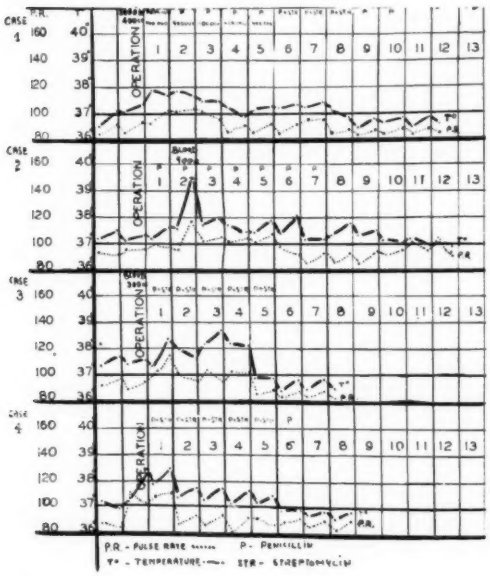
It is important to emphasize several points in the use of this method. After evacuation of the cyst and resection of the redundant parts of the adventitious fibrous capsule, the cavity in the liver is obliterated by omentum and peritonealized. Resecting the capsule instead of suturing it will prevent fluid accumulation and possible secondary infection. Figure 1 is a roentgenogram of postoperative fluid-filled cysts. The cysts in this case were evacuated and closed without resection. The fluid remained in the cavities for almost a month.

The present technic is not applicable in all cases of hydatid cyst of the liver. In cysts with secondary infection and communication with bile passages, marsupialization remains the method of choice. In cases with exogenous proliferation of parasitic diverticula, Costantini and associates[4] have proposed resection of the adventitious fibrous capsule. This type of hepatic hydatid disease, however, is rare, Costantini having seen no cases during 25 years of careful observation.[4,5]

The technic proposed here has the advantage of a low and brief morbidity. The reported patients remained in the hospital 8 to 12 days after operation. They returned to active normal living.

With the method of marsupialization, 10 patients operated on in our hospital had an average stay of 37 days and required further ambulatory treatment for months because of abdominal fistulas.

FIGURE 1. Roentgenogram of postoperative fluid-filled cysts.



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Coccidioidomycosis

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Coccidioidomycosis is a common disease and can be found throughout the country because of the many troops exposed to Coccidiodes immitis, *the etiologic fungus, during the war, and also because of the many visitors exposed since the war as a result of residence in or travels through the endemic areas in the southwestern part of the United States. The disease is reviewed, including mode of infection, clinical course, laboratory and radiographic findings and treatment.*

SCHWARTZ and Muth[1] recently published an excellent review of the subject of coccidioidomycosis. An earlier excellent summary was presented by Smith.[2] We have reviewed all the cases of coccidioidomycosis diagnosed from April 1946 to April 1951 at the Veterans Administration Hospital at Van Nuys, California, and later at Long Beach, after the Van Nuys installation was transferred there. There were 39 cases in the five year period.

Age and sex—All the patients were men, and their ages varied from 21 to 60 years.

Onset and symptoms—Upper respiratory symptoms were noted by 17 patients (44 per cent) and were questionable in 4 others. Chest pain was noted in 17 cases, and hemoptysis in 7 (18 per cent). Four patients (10 per cent) had erythema nodosum on admission. In a series of 100 cases, Willett and Weiss[3] noted fever in 80 per cent, chest pain in 74 per cent, cough in 64 per cent and malaise in 43 per cent (Figure 1). Goldstein and Louie[4] noted chest pain in 95 per cent of their cases, with hemoptysis in 21 per cent.

Coccidioidin skin test—This test was positive in 30 cases (88 per cent of those in which this observation was recorded) and negative in 4. In 2 of these 4 cases there was x-ray evidence of a cavity; 1 patient had coccidioidal pneumonia with a small pleural effusion, and 1 had a cavity which was complicated by empyema following treatment elsewhere by means of pneumothorax.

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LEROY HYDE

CHARLES POKORNY

BERNARD HYDE

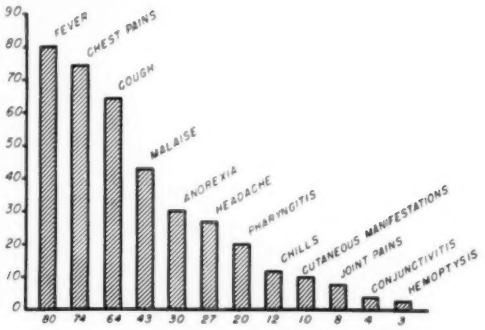

FIGURE 1. Frequency of symptoms in 100 patients hospitalized for pulmonary coccidioidomycosis. (Modified from Willett and Weiss.[3])

Smith and co-workers[5] in an excellent review of the use of coccidioidin noted that the skin test becomes positive usually 10 to 14 days after infection, with a range of 7 to 28 days. Of 462 clinical cases of nonprogressive coccidioidal disease, all patients reacted to 1:100 coccidioidin. However, only 30 of 100 patients with coccidioidal dissemination reacted to this dilution.

Other laboratory tests—Leukocytosis and elevation of the sedimentation rate may be found frequently. Eosinophilia (more than 4 per cent eosinophils in differential blood smear) was noted in 71 per cent of our cases. Sweigert[6] reported eosinophilia of from 10 to 29 per cent in 23 per cent of his patients.

Dissemination—This occurred in 7 (18 per cent) of our patients. In our small group, Negroes seemed most vulnerable (Table 1), although Smith has found Filipinos to have the highest rate of dissemination (Table 2). It appears that dissemination occurs more frequently among darker skinned persons than among Caucasians.

X-ray findings—Of these 39 hospitalized patients, 34 (87 per cent) had roentgenographic evidence of bronchopneumonic densities of varied size, 5 had cavities either isolated or with surrounding bronchopneumonia, and 2 had prominent hilar adenopathy. Five patients had normal chest films when seen by us; these included 2 patients with dissemination and 2 who had coccidioidal meningocephalitis.

Discussion

Coccidioidomycosis is a fungous disease, endemic to large areas of the southwestern part of the United States. Chlamydospores or arthrospores, the infectious "vegetative" form of *Coccidioides immitis*, enter the body through the respiratory tract—usually through the air but occasionally on clothing or other dust-contaminated objects. The arthrospores develop into double refractive spherules which reproduce by endosporulation (Figure 2). Infection is more common during dry, dusty seasons (July through October). Endemic areas include California (mainly the southern San Joaquin Valley, but also areas in San Bernardino and Riverside counties), southern and central Arizona, southern New Mexico and western Texas (Figure 3). The incubation period is one to three weeks—usually 10 to 16 days. The disease is not infectious.

The primary pulmonary infection usually is asymptomatic, localized and self-limited. The usual course is uncomplicated healing of the primary lesion, occasionally with fibrosis and calcification. The only evidence of infection may be a positive coccidioidin skin test (Table 3).

Coccidioidin, a cultural extract, is a valuable aid in diagnosis. Smith's[5] preparation, which he has kindly supplied for our use, was

TABLE 1

COCCIDIOIDOMYCOSIS; INCIDENCE OF DISSEMINATION IN 39 CASES

RACE	TOTAL CASES	DISSEMINATION
Caucasian	26	3
Filipino	5	1
Negro	4	3
Mexican	4	0
TOTALS	39	7 (18 per cent)

TABLE 2

COCCIDIOIDOMYCOSIS; INCIDENCE OF DISSEMINATION*

RACE	PER CENT INCIDENCE
Caucasian	0.2
Mexican	0.7
Negro	2.8
Filipino	36.0

*Based on data from Schwartz and Muth.[1]

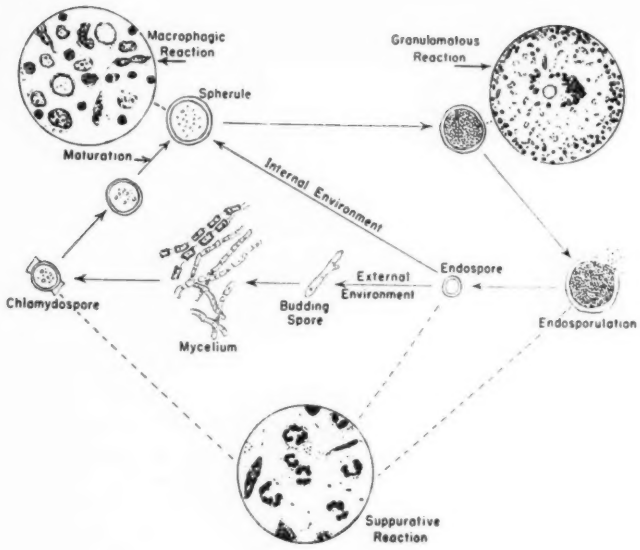

FIGURE 2. Life cycle of *C. immitis* and related histologic response. (From Forbus and Bestebreurtje.[8])

chosen from varied lots after those extracts causing nonspecific reactions were discarded. Several strains of *Coccidioides* were used as inoculums to secure an antigen with a broad yet specific spectrum. Dilutions of 1:100 are used except for patients with erythema nodosum, in whom dilutions of 1:1000 are preferable.

Sensitization due to repeated skin tests with coccidioidin does not occur.[5] The skin test becomes positive in man from 10 to 45 days after exposure, usually during the second or the third week following inhalation of arthrospores. However, up to two-thirds of the patients with disseminated coccidioidomycosis fail to react to 1:100 dilutions of coccidioidin. Our experience agrees with that of Smith: "When the coccidioidin test has been performed, if it is positive, and there is clinical evidence of an active coccidioidal infection, which is not disseminated, serological tests may be useful. If dissemination is suspected, even a negative coccidioidin warrants these follow-up tests. In view of the persistence of coccidioidin sensitivity, a mere positive coccidioidin is no indication for serological tests. Moreover, unless dissemination is suspected, a negative coccidioidin should screen out the serological test. In patients who do not disseminate, the humoral antibodies are not present prior to the development

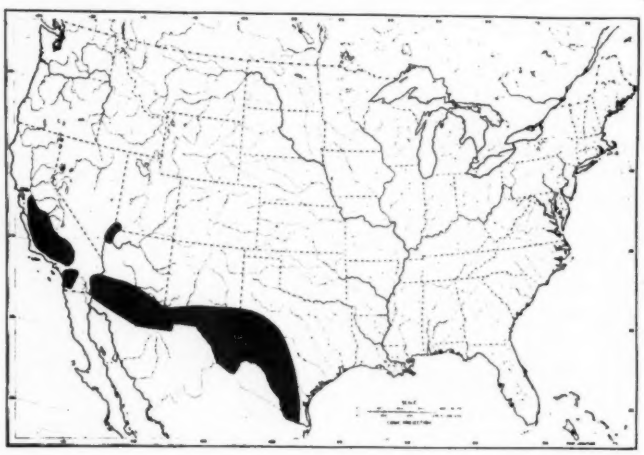

FIGURE 3. Known coccidioidal endemic areas in the United States. (From California Med. 75:387 [December] 1951.)

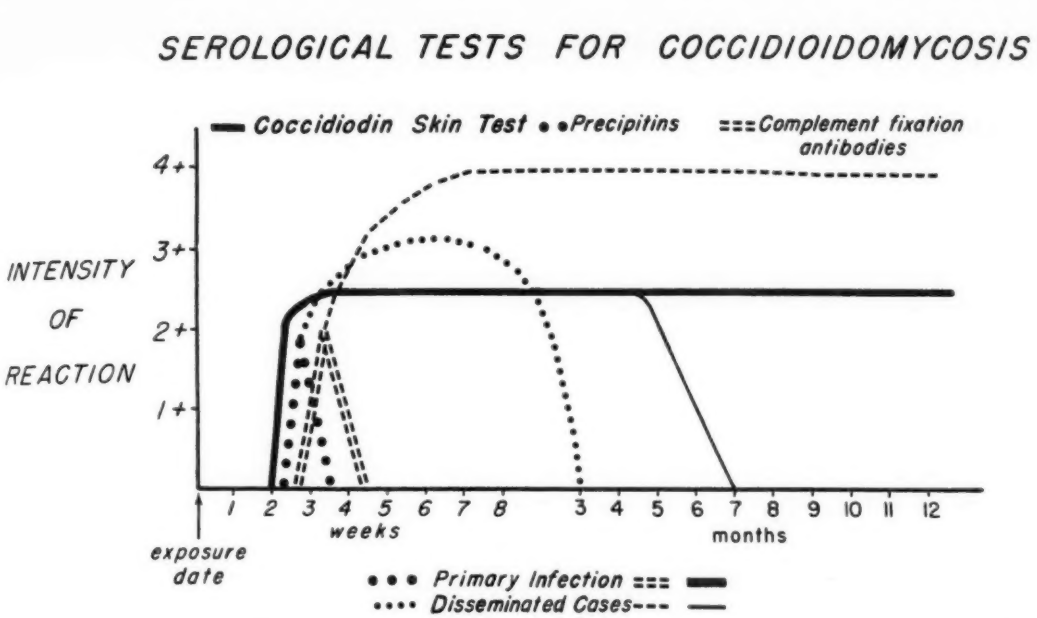

FIGURE 4. Schematic graph illustrating relationship of coccidioidin skin reaction and serologic tests in primary and disseminated infections.

of coccidioidin sensitivity. With very mild infections, serology may never become positive. Generally, precipitins develop earlier and vanish sooner than do the complement fixing antibodies. The latter appear to have important prognostic value, for only rarely are they negative in progressive disease" (Figure 4).

Initial primary infection is nearly always pulmonary and well localized (Table 3). Sixty per cent of the patients are asymptomatic, and the infection is recognizable only by development of sensitivity to coccidioidin. Another type of infection produces symptoms of upper respiratory disease or influenza. The fungus may be found in the sputum, and the reaction to the skin test with coccidioidin usually becomes positive. A roentgenogram of the chest may reveal a pulmonary lesion (bronchopneumonia), enlarged hilar lymph nodes and occasionally pleural effusion. About 5 per cent of patients have an episode of erythema nodosum or erythema multiforme.

The diagnosis of coccidioidomycosis can be established definitely by isolation of the fungus *C. immitis* on culture. The presence of coccidioidal complement fixation antibodies or precipitins in the blood serum is also diagnostic. The finding of a positive coccidioidin skin test indicates either present or past infection, and alone is not diagnostic of active disease. However, conversion from a negative to a positive skin test indicates active coccidioidal infection. Fatigue and malaise are noted regularly, and pleural pain has been found in

TABLE 3

COCCIDIOIDOMYCOSIS: SUMMARY OF FINDINGS (INITIAL OR PRIMARY INFECTION)

1. Unapparent and asymptomatic. Usually recognizable only by development of sensitivity to coccidioidin—60 per cent of cases
2. Acute respiratory or influenza-like illness with malaise, chest pain, cough, fever, hemoptysis, etc. X-ray often reveals pulmonary lesion. Usually bronchopneumonia
3. Erythema nodosum or erythema multiforme found in 2 to 5 per cent of all cases, and occurs when sensitivity to coccidioidin is established (usually one to three weeks following exposure to *C. immitis*)

45 to 85 per cent of symptomatic patients. Fever occurs in 60 to 100 per cent of cases. Minimal hemoptysis has been noted in about 28 per cent of patients.

The clinical history and gross pathologic features of coccidioidomycosis are similar to those of pulmonary tuberculosis. Comparative roentgenograms may be indistinguishable. The cause of a given pulmonary lesion is often clarified by the isolation of specific organisms.

Four types of roentgenographic findings have been noted: (1) by far the most common, a nonspecific bronchopneumonic density, varying in size but usually less than one-third or one-fourth of a lung field; (2) cavities, often thin-walled. These usually develop within a bronchopneumonic density so that the thickness of the cavity "wall" depends on the amount of surrounding pneumonia, at least early in the disease. These cavities usually do not produce symptoms or require treatment; (3) hilar adenopathy occurs frequently and is very suggestive in a patient who has been in an area endemic for coccidioidomycosis; (4) a small, dense nodule, coccidioma, which represents the healed, fibrotic residuum.

Disseminated coccidioidomycosis is a rare complication, occurring once in about 750 cases. Dissemination may occur during the primary infection or somewhat later; it is more common in darker skinned persons such as Mexicans, Negroes or Orientals, occurring once in every 40 cases of infection in male patients.[7] The mortality rate is about 50 per cent. Progressive dissemination is nearly always manifested within a few months after the initial primary infection and often with no interlude, as emphasized by Smith. Occasionally, however, there is some interval between the primary coccidioidal infection and subsequent dissemination.

Treatment

Treatment varies with the stage of the disease. Primary coccidioidal infection produces no symptoms in 60 per cent of cases, and these patients often do not seek medical care. Most of the remainder will require mild symptomatic therapy such as aspirin for headache, codeine for chest pain, etc. Bed rest is indicated during the febrile period. The coccidioidal pulmonary cavity almost never requires therapy. The situation must be explained to the patient to avoid anxiety and iatrogenic disability. The patient is permitted to lead a completely normal life and is told about the possibility of blood-streaking or hemoptysis. Patients with recurrent, disabling hemoptysis require lobectomy. (It must be noted that in rare instances new cavities may develop in the remaining lung tissue after lobectomy.)

With dissemination, treatment is ineffective at the present time. A long list of drugs which have been used includes arsphenamine, gentian violet, thymol, antimony, potassium tartrate, sulfonamides, iodine, histamine, colloidal copper, penicillin, AUREOMYCIN® and streptomycin, but these are of no value. Prodigiosin appears to have value in vitro but no apparent value in patients clinically. Also fungistatic in vitro are streptothricin and plumbagin, which, however, cannot be used parenterally. Bed rest and general supportive measures seem as efficient as any drug therapy to date. The newest drug being tested is C-131 or nynstatin. When used in animals, this drug appears to cure disseminated coccidioidomycosis whereas the control animals die.[9] Further studies are in progress and the results in patients are awaited.

Grateful acknowledgement is made to the Department of Medical Illustration, Rosebud Lane Preddy, Thomas Masterson, Frank Grossman and Timothy Dodge for charts, tables and illustrations, and to Lucy Montana for secretarial assistance.

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Cancer of the Stomach

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The present attitude toward carcinoma of the stomach is one of aggressiveness. Surgery is not an ideal treatment by any means, but it is the only treatment at present, and on the basis of results the author feels that there is justification for extending the scope of surgery rather than becoming more conservative.

STANLEY O. HOERR

THE attitude toward carcinoma of the stomach is one of increased aggressiveness. It is manifested by a desire to obtain a tissue diagnosis in every case, irrespective of how hopeless the situation may seem to be, because a certain proportion of patients will have a radiosensitive lymphoma. It is manifested by an unwillingness to accept the criteria of inoperability that were in force a decade or two ago because today we are able to do more extensive resections.

Presentation of Patients

Case 1—Our first patient, a farmer, was operated on by Dr. Thomas Jones in 1945. He presented himself because of epigastric pain and loss of appetite of four months' duration. He had lost 25 pounds.

Physical examination disclosed a mass in the left epigastrium. Some of you will recall when a palpable mass was regarded as a sign of inoperability in carcinoma of the stomach. Gastric analysis revealed no free acid, with 12 units total. Hemoglobin was 61 per cent—it should have been 85 to 90 per cent. Plasma proteins were reduced. Roentgenograms that he had brought with him from his family physician showed what was interpreted as a large polypoid carcinoma of the stomach.

I would like to read from Dr. Jones' operative notes: "The abdomen was entered through an upper midline incision. The stomach presented a large neoplastic mass involving the middle half and extending up to 1 inch below the esophagus. The lesion grew directly into the midtransverse colon and extended back toward the pancreas but without actual invasion of the pancreatic tissue. There was no Blumer's shelf and the liver was negative. The entire stomach was removed and the transverse colon was removed and a Mikulicz resection done."

The colostomy was closed at a later date. The pathologic report was as follows: sessile, polypoid, ulcerated, moderately well differentiated adenocarcinoma of the stomach with invasion of the entire wall and direct extension into the transverse colon; chronic atrophic gastritis; chronic colitis; acute and chronic hyperplastic lymphadenitis; no lymphatic metastases.

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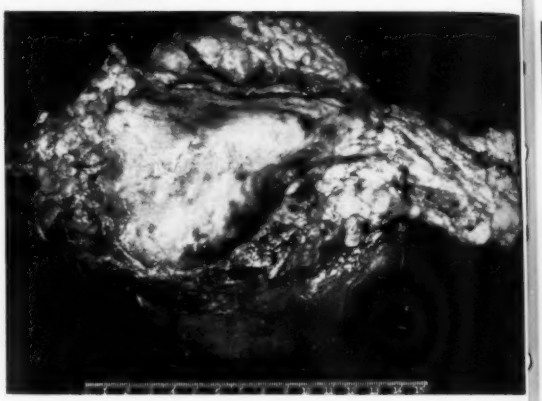
Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

FIGURE 1 *(left)*. Preoperative roentgenograms of 40 year old man (Case 2). Large cancer of upper half of stomach.

FIGURE 2 (Case 2) *(below)*. Specimen removed includes upper three-fourths of stomach, several inches of esophagus, spleen, part of the tail of the pancreas, part of the left lobe of the liver and part of the diaphragm.



Today this patient enjoys vigorous health. He tells me he works 14 to 16 hours a day on his farm. He eats six meals a day, and the only thing that doesn't agree with him is a second helping. Before he became ill he averaged 155 pounds in weight, and now he weighs 140. That is characteristic of patients who have radical resection of the stomach; they rarely are able to regain their original weight, although most of them feel perfectly well, and of course according to life insurance companies it is better to be underweight than overweight.

He takes some medication in the form of hydrochloric acid and pancreatin, and every couple of weeks his family physician gives him a liver injection. His blood count has remained normal.

Dr. Arthur Allen taught me to ask the following question of patients who have had good results from total gastrectomy: Was it two or three years before you felt like yourself again? This patient tells me it was between two and three years, again a characteristic finding. Removal of the entire stomach or a large portion of it is not a benign procedure by any means, and it takes a long period of readjustment before the patient feels perfectly well. Usually, however, the patient is so grateful to be rid of the symptoms caused by the lesion that the discomfort of doing without a stomach is relatively slight and he is more than willing to make the dietary compromises necessary.

Case 2—This 42 year old man was first seen approximately two years ago. For about a year prior to that time he had been highly nervous and had no appetite. He had lost about 40 pounds in weight. For four months before his first visit he had become increasingly nervous, and had had pain across the abdomen and vomiting. In my experience, pain associated with carcinoma of the stomach means one of two things: an ulcerated carcinoma or extension into adjacent organs. A nonulcerating carcinoma confined to the stomach ordinarily will be painless.

Physical examination was essentially negative except for evidence of loss of weight. It was the impression of the examiner that he suffered from an acute anxiety state. The statement was made in the report that "I doubt that we will find very much organic disease but we will check closely." Gastric

analysis showed 40 units of free acid, and the hemoglobin was 9.8 gm.

A preoperative roentgenogram showed an extensive neoplasm involving the upper half of the stomach, right up to the esophagus (Figure 1).

Operation was done in June 1950, and consisted of a large block resection for a neoplasm involving the upper half of the stomach and extending into the pancreas, diaphragm and left lobe of the liver (Figure 2). By cooperation with the pathologist it was possible to reach apparently normal margins of tissue in all organs.

Postoperative films taken about a month after surgery (Figure 3) show the esophagogastrectomy with the lower quarter of the stomach remaining. The increase in size of the gastric stump is shown over a two year period. One can see the advantage to the patient of leaving even a small remnant of stomach.

This man went back to work seven weeks after operation. He works at a steel mill, casting steel, and his working days are long—15 hours. His highest weight before operation was 180 pounds, and he now weighs 120 pounds. He states that he feels well except "when I work myself hard it takes a little longer to recuperate than it used to."

This patient is well aware of the circumstances of his operation. We got around his tumor by a rather narrow margin, but I think there is considerable reason for optimism.

FIGURE 3 *(left)*. Postoperative roentgenograms, Case 2. Film on left taken one month postoperatively; film on the right taken two years postoperatively. These roentgenograms illustrate the increase in size which a gastric stump will undergo with the passage of time.

FIGURE 4 *(below)*. Preoperative roentgenogram, Case 3, man, aged 52. Large cancer involving most of stomach.

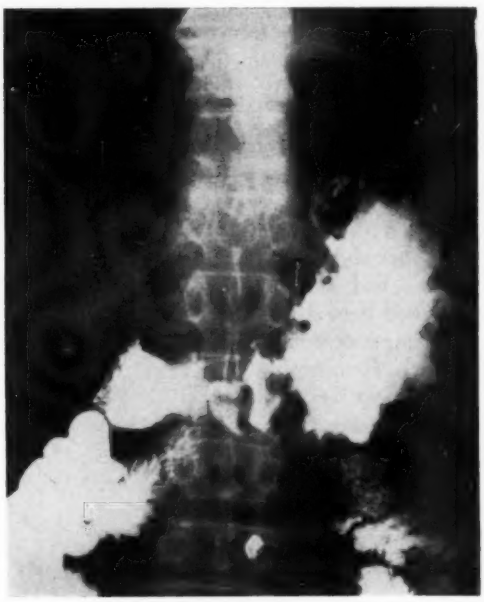


FIGURE 5 (Case 3) *(right)*. Specimen removed includes all but the last centimeter of stomach toward the esophagus, spleen, tail of the pancreas, mesocolon and transverse colon, and section of abdominal wall.

FIGURE 6 *(left)*. Incision employed, Case 3. Oblique incision adapts itself well to intrathoracic extension if it becomes desirable to open the chest for a high cancer of the stomach.

FIGURE 7 *(below)*. Postoperative roentgenogram, Case 3. Gastric cuff has been anastomosed to duodenum. The resection produced a "functional" total gastrectomy, but not quite an "anatomic" total gastrectomy.

This is an example of what you might call radical neighborhood surgery where the adjacent organs are removed. I think it is the feeling of most persons today that a total gastrectomy is not necessary in every case of carcinoma of the stomach. The important thing is to get an adequate margin of stomach wall and also any organ to which the lesion is adherent.

Case 3—This 54 year old man, also a factory worker, was seen in July 1950. He had been ill for about seven months, again with pain as a feature of his difficulty—pain in the left upper abdomen. For three or four months he had had anorexia and dark stools, and there had been a loss in weight of 25 pounds.

Roentgenograms showed carcinoma of the stomach. Hemoglobin was 12 gm., and physical examination disclosed a questionable abdominal mass. The preoperative roentgenogram (Figure 4) shows irregularity of the two curvatures of the stomach representing a large tumor which extends almost to the esophagus.

We operated on him in July 1950. The tumor was found to be adherent to the abdominal wall, the pancreas, the spleen and the mesocolon (Figure 5). Experience has shown that when a tumor involves the transverse colon it is usually the mesocolon rather than the colon proper. In Case 1 it was the colon, but the mesocolon can be removed quite conveniently and whatever vessels are necessary may be sacrificed. The operation can be completed and it can be determined whether the blood supply to the colon has been permanently injured. In this patient it was necessary to resect the transverse colon as an encore to this procedure. Fortunately he is a relatively thin person and therefore everything went very satisfactorily. It was possible to save a 1 cm. cuff of stomach. That centimeter cuff of stomach, when it can be preserved, is very useful to the surgeon because the stomach makes a safer anastomosis than esophagus.

This man eats between 4 and 7 meals a day, and works very hard. Aside from greasy

foods, he has no difficulty eating. He has been kind enough to talk with patients of mine who have had total gastric resections and have experienced some of the initial difficulties that go with absence of the stomach, and he has encouraged them.

No lymph nodes were involved in this case, and the outlook is favorable.

Figure 6 illustrates the incision which was employed. Where we anticipate a high resection it is convenient to use an oblique incision so that if necessary it can be continued into the chest and the chest opened widely.

With every large resection involving the stomach and adjacent organs it usually is advisable to put a small rubber tube into the jejunum for use in supplementary feedings for as long a period as necessary, should there be difficulty in the anastomosis. One patient of mine had an anastomotic leak, and we fed him exclusively by jejunostomy tube for five or six months because a stricture developed. Later we were able to resect the stricture, and he survived.

In Case 3 we were able to hitch the cuff of stomach directly to the duodenum, so this patient has in effect an esophagoduodenostomy. A postoperative roentgenogram is shown in Figure 7.

Case 4—Our fourth patient underwent operation in June 1951. She is a 45 year old mother of five children, and works eight hours a day in a factory in addition to being a homemaker. When we first saw her she had had eight months of severe gnawing pain in the right and left upper quadrants. She had had a diagnosis of nervous indigestion, but her family physician wisely advised an operation even though the roentgenographic findings were not conclusive. Our first impression was that we were dealing with a case of nervous exhaustion and that there might possibly be a peptic ulcer or Addison's disease.

Roentgenograms suggested a gastric ulcer (Figure 8). We couldn't be sure whether it was benign or malignant. At operation the tumor was found to involve the entire stomach. The spleen, about half of the pancreas, and the transverse mesocolon were removed because of extension of the lesion. She did very well postoperatively. None of 34 lymph nodes were involved, so the outlook is optimistic in spite of the extensive resection.* She weighed about 137 pounds prior to her illness, and she now weighs 90 to 100 pounds.

Discussion

A study of the rate of operability shows

*Since this presentation ascites has developed which has proved to be due to carcinomatosis.

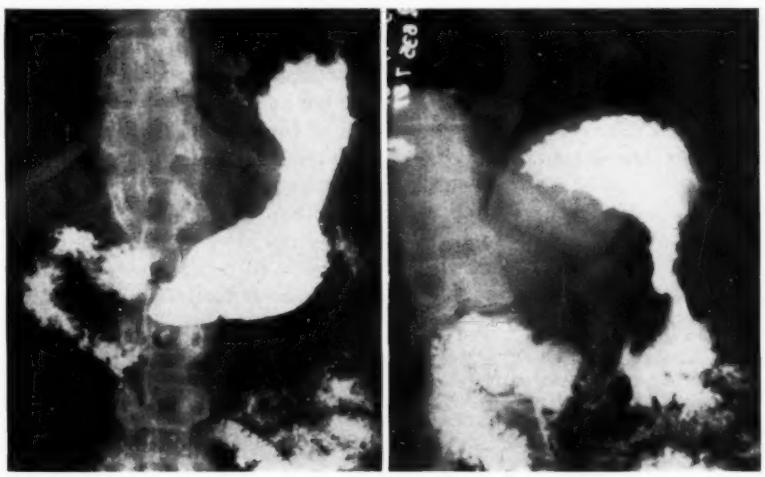


FIGURE 8. Preoperative roentgenograms, Case 4, 43 year old woman. Ulcerative lesion of the middle third of the stomach is shown, but the true extent of the lesion cannot be gauged from these films.

that roughly 90 per cent of patients with gastric malignancy undergo some type of surgical procedure. It may be merely a biopsy of a supraclavicular node or a liver biopsy, but it does establish a tissue diagnosis. In the past 10 years the rate of gastric resection per hundred patients operated on has doubled, from 25 to 50 per cent. The additional resections represent for the most part complicated procedures in which the entire stomach or adjacent organs are removed.

The basis for urging a tissue diagnosis in each case is to be found in Table 1, where it is seen that about 10 per cent of all gastric malignancies are radiosensitive. Lymphosarcoma is a radiosensitive tumor which in many instances permits a five year survival with adequate treatment, no matter how hopeless the situation seems at the time of operation. Reticulum cell sarcoma likewise is quite radiosensitive, as is also Hodgkin's granuloma. The outlook in a case of Hodgkin's sarcoma is very bleak. A leiomyosarcoma may grow very slowly, so even a massive tumor of this type may be successfully removed with periods of arrest of 5 or 10 years.

If a gastric ulcer is at all suspicious it should be removed by resection, because this is good treatment even if it is only an ulcer and because the chances of cure if it is cancer are much higher than in cancer of the stomach as a whole. In 19 patients with diagnoses of gastric ulcer—malignancy or benignancy undetermined—it was possible to do a resection for cure in 15 of them. In the entire series of gastric malignancies it was possible to attempt a resection for cure in somewhat less than half the patients.

There is a corollary to this viewpoint. If you do explorations in a large group of patients with gastric ulcer you have to be able to show that there is a reasonably low mortality rate if the condition proves to be benign. In a series of 79 operations for possible gastric malignancy there was 1 death. I do not think that is too great a risk to ask patients to take, when the malignancy, if present, will be in a favorable phase.

The sigmoidoscope has been found to be quite useful in exploring the stomach in some cases. We have it sterilized, make an opening in the stomach, insert the instrument, clamp it off and take up the slack in the stomach with a Babcock clamp so we can inflate the stomach with air and do a transabdominal gastroscopy, and get views of the stomach, particularly the fundus, which are impossible to obtain by any other means. High fundal lesions are difficult to detect by conventional methods and there may be lesions which cannot be seen or palpated from the outside, so before a patient suspected of having a carcinoma of the stomach is regarded as being normal, I think the surgeon should take a look at the inside of the stomach with some such instrument as the sigmoidoscope.

TABLE 1

GASTRIC MALIGNANCY; PATHOLOGIC CONDITIONS IN 102 PATIENTS

Carcinoma	88
Lymphosarcoma	7
Reticulum cell sarcoma	3
Leiomyosarcoma	3
Hodgkin's disease	1
	102

MEETINGS AND POSTGRADUATE COURSES

University of Minnesota, Minneapolis: Continuation course in dermatology for practicing physicians, November 19-21, 1953, at Center for Continuation Study. Recognition and management of common skin disorders will be stressed. The program will be presented under the direction of Dr. H. E. Michelson, Professor of Medicine and Director of Dermatology. Remainder of the faculty will be drawn from University of Minnesota Medical School and Mayo Foundation.

University of Minnesota: Continuation course in fractures, November 16-18, at the Center for Continuation Study. Intended primarily for general practitioners, the program will emphasize management of common fractures and some frequent complications. Guest speakers will be Dr. Edwin F. Cave of Massachusetts General Hospital and Dr. Walter P. Blount of Milwaukee County Hospital. Dr. Wallace H. Cole is director of the course.

Cardiac Clinic on Hypertension

ARTHUR M. MASTER*

Mount Sinai Hospital, New York City

By essential hypertension is meant an increase in arterial tension without a definite cause. Excluded, therefore, is hypertension due to kidney disease, adrenal tumor, eclampsia, coarctation of the aorta, cerebral compression, etc. This paper discusses the clinical findings of hypertension or hypertensive heart disease, but also includes a cardiac clinic on "New definitions of normal blood pressure and hypertension."

ARTHUR M. MASTER

INCLUDED in this clinic are brief discussions on questionable hypertension, definite hypertension, malignant hypertension, and hypertension and chest pain. I would first like to say that the definition of hypertension is of practical importance. There is a high blood pressure phobia in this country. Every physician takes a blood pressure reading at practically every examination, whether the patient is applying for insurance, has a cold, is being examined for military service or for employment, or is undergoing a regular annual checkup. If an infection is present, the first thing done is a blood pressure determination; if there is a hernia, the initial study is the blood pressure.

What constitutes high blood pressure? The generally accepted upper limit of normal is 150/90, but in a 20 year old man a systolic reading of 140 may be an indication of high blood pressure. In a 70 year old man, on the other hand, 150, 160, 170 or even 180 may be entirely normal.

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Presented before the thirty-seventh annual Assembly of the Interstate Postgraduate Medical Association at Cleveland.

The first of 4 patients to be presented is Mrs. R., who is 65 years old and whose chief complaint is dizzy spells. She has had intermittent high blood pressure for 8 to 10 years. She tells me that for the past year her blood pressure has been 290. She has received hypertensive drugs and she has been hospitalized. During a week in the hospital, the blood pressure did not go above 145 systolic and 85 diastolic. Of course that raises the question of pheochromocytoma. Perhaps right now she is in the phase where there is no increase in arterial tension. She has had two histamine tests, with no rise in blood pressure. With a cold pressor test, the rise was not significant. Thus the laboratory aids have not helped. Drugs like regitine and benzodioxane cannot be assayed now, because the blood pressure is normal.

A chest roentgenogram and an electrocardiogram are negative. The retinal vessels are essentially normal. It is hard to square the history of a 290 blood pressure with the clinical findings. A systolic reading of 290 at the age of 65 would be hypertension, no matter

what definition were employed. Dizziness, of course, is a common complaint of patients with hypertension.

Let's discuss the next case for a few moments. This 50 year old man, Mr. W., is head locker-room man at a club, and although that may sound easy, it is hard work. He works 12 or 14 hours a day and says he always "drives" himself. By the way, these patients know their blood pressures, so whether you believe in revealing blood pressures to patients or not, we repeat them here because they appear to know them. I always tell a patient frankly that he has high blood pressure, but I don't tell him how high it is. I don't like my patients to worry. If I can get them to relax, I think I will have more therapeutic success than by use of hypertensive drugs. When I was speaking with these 4 patients in the anteroom, I kept telling them that they looked too serious, that each had a "sour puss," in the hope that they would relax a little.

Routine examination on August 28 showed Mr. W.'s blood pressure to be 230/140. In any man's language that is hypertension. It doesn't seem likely that he has had it for a long period of time, because roentgenograms show his heart to be of normal size. The electrocardiogram is essentially normal. There is a left axis deviation and the T_1 is small, but there is no typical pattern of left ventricular strain. What I am trying to say is that when you are in doubt as to the presence of hypertension, roentgenograms and electrocardiograms can be of help. In this case, however, they certainly don't show much.

He does not have pheochromocytoma. His blood pressure didn't drop on test. He was given APRESOLINE®, 50 mg. orally four times a day, slowly increased to 200 mg. four times a day; no effect was noted. Many investigators have found that combinations of these drugs are effective when a single drug is not. So about two weeks ago he was given hexamethonium, 375 mg. four times a day, and apresoline, 125 mg. On this combination his systolic blood pressure has decreased to 200; the diastolic has remained at 140. Mr. W. states that he feels fine.

When you administer hypotensive drugs it is wise, particularly in the doses I mentioned, to keep the patients in the hospital so you can observe them. They develop a postural hypotension on standing and therefore have a tendency to faint. These patients here today are allowed to walk around but are kept near the beds. Mr. W., would you mind pulling up your trousers and showing us the leggings you are wearing? He is wearing an ACE® bandage to prevent postural hypotension when he stands.

Mr. W. has no enlargement of the heart; his electrocardiogram shows no left ventricular strain; there is no kidney damage. Here is a man with essential hypertension, whose heart and kidneys are functioning normally.

Mr. S., the third patient, operates a lift which elevates luggage into an airplane. He is 45 years of age. In 1943, at the age of 37, he first learned that he had high blood pressure. His systolic reading was 165, and he was rejected by the Army. In 1947 he had dizzy spells and complained of headaches. His blood pressure in 1948 was 190; in 1949 it was more than 200 systolic. We don't have the diastolic readings. Also in 1949, he began to complain of nausea and vomiting. For the past three years, however, his chief complaint has been headache.

Seven or eight months ago he complained of difficulty of vision, with blurring. The following month nocturia developed and a prostatectomy was done. I thought at first that he might have had the prostatectomy in the hope that it would help the hypertension, but apparently the operation was done for prostatism. Incidentally, this procedure did not change the hypertensive picture.

Three months ago there was onset of weakness, nausea and vomiting. I think you can read between the lines of this report and suspect that the kidney was involved and that he might have increased blood nitrogen. He has lost 25 pounds in the last 11 months.

He has received apresoline, hexamethonium and compounds of veratrum viride—in what doses we do not exactly know. He was admitted to the clinic a month ago, and his blood pressure at that time was 230/158. The

retinas showed papilledema, hemorrhages and exudates. So you see he certainly has hypertension. A roentgenogram is typical of hypertension. Of course, in a case like this, no roentgenologic study is required to establish the diagnosis; from the clinical findings—the eye changes, kidney impairment and elevated blood pressure—it is obvious that he has hypertension. Were you in doubt, however, you might learn whether hypertension is present by looking at an x-ray. An enlarged heart, a left ventricular enlargement, and a tortuous aorta are characteristic. An electrocardiogram also can be helpful. In this man's case it shows left axis deviation, high voltage RST changes in lead I and the chest lead, with T_1 inversion—a typical pattern of left ventricular strain. Thus the combination of papilledema of the retina, electrocardiographic findings and roentgenographic changes indicates long-standing hypertension whether the systolic blood pressure reading is 230 or 160.

A benzodioxane test and a regitine test were done to exclude pheochromocytoma, but as you might already have guessed, these were negative; such a definite hypertension is not due to an adrenal tumor.

Last month the patient was given a combination of drugs that Schroeder has recommended, a combination of 235 mg. hexamethonium and 100 mg. apresoline, four times a day. He has postural hypotension on standing. He also is wearing an ace bandage to prevent postural hypotension and fainting while he is standing. Although he is ambulatory, he keeps near his bed so that he can grasp support if necessary. During the past week he has been definitely improved. The blood pressure now is 190/110. The retinal exudate, hemorrhages and papilledema have decreased since he has been hospitalized and received hexamethonium and apresoline. He tells me that he feels much better, that his headaches have almost disappeared and that his vision is improved. When he was admitted to the clinic, he was unable to read; now he says he can read a little, so there is some improvement.

Our last patient is a 55 year old man who, unlike the other 2 men presented, has a relatively easy job, that of operating an automatic machine. Incidentally, the lady here, too, told me she always had a "drive," and that, of course, frequently is associated with high blood pressure. If you can get the hypertensive patient to lead an equable existence, mentally and physically—and you often can, if you can show them the need to be philosophic—you will be successful in many cases.

This man was presented to me as a person who complained of chest pain and who had an anginal syndrome, but he also has hypertension, as you will see. He has pain in the neck and in the upper chest following any exertion—walking, eating, exposure to cold, excitement. Here is a classic picture of a Heberden's angina.

In 1947 he noted that he became short of breath on exertion. He has known for a few years that he has high blood pressure. In April 1951 it was 190/120—for a man of 55 years this is hypertension by any definition. But if this man of 55 had a blood pressure of 155, would that be hypertension? Suppose he had 160, 165 or 170, and suppose further that he had no complaints and that you could find no objective evidence of disease, would that be hypertension? I will say more about that later.

He was admitted to the clinic two and a half weeks ago, not only because of the chest pain but also because of a rapid pulse, congestion of the lungs and auricular fibrillation. It is interesting that during this period of auricular fibrillation his blood pressure dropped to 132/80. Blood pressure often falls when auricular fibrillation sets in. The patient was in heart failure. He had been digitalized before admission to the clinic. After his admission, the amount of digitalis administered was increased to 0.2 gm. a day, and he was placed on quinidine, 0.6 to 0.8 gm. four times a day throughout the 24 hours in an attempt to regularize his heart. In a patient with an enlarged heart, such an attempt usually is not successful, but in my opinion this was the correct procedure; the auricular fibrillation was very recent, and in such a case you may be successful in changing the arrhythmia to a regular sinus rhythm.

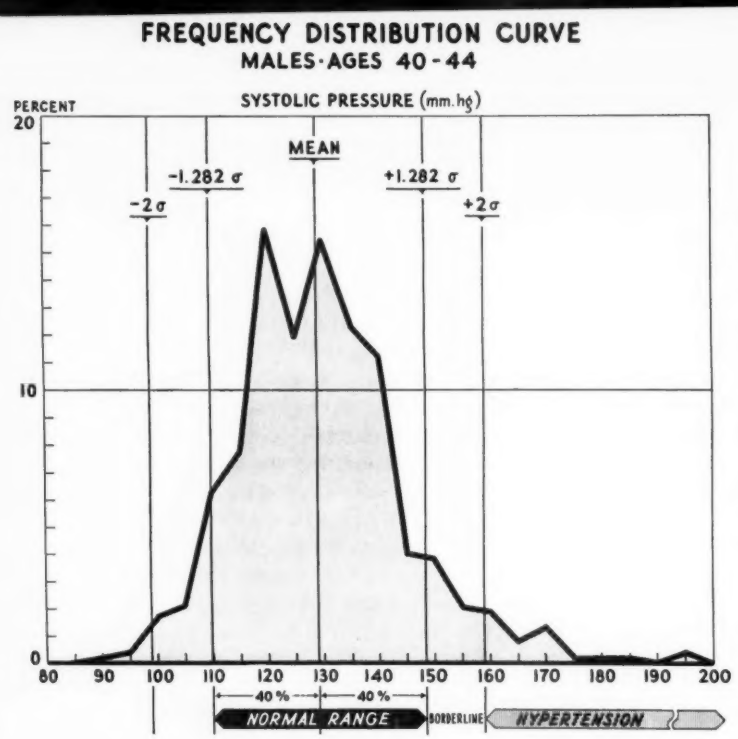

FIGURE 1.

The rhythm became regular five days ago, and now the patient is on a maintenance dose of 0.1 gm., that is, 1 cat unit or 1.5 gr. of digitalis leaf daily, and 0.4 gm. (6 gr.) of quinidine four times a day. His pulse rate is 64. Here, then, is a case of combined hypertension and angina pectoris due to coronary disease.

This man is not ambulatory. He tells me he has very little pain now, so long as he is at rest. After he eats or gets excited or walks, there is pain. He had not taken nitroglycerin until he was admitted to the clinic.

The story of this patient is quite typical. Surely in a 55 year old man who has pain in the upper chest radiating to the neck which develops following effort, excitement, cold and meals, and is relieved by nitroglycerin, the chances are 100 to 1 that coronary disease is present. But may I leave this thought with you: Not every patient with coronary disease presents such a picture. At least 10 per cent of patients with definite coronary disease do not have the classic angina syndrome. Don't always expect pain in the midline; it may be in the precordium. Don't always expect pain on effort and excitement, or pain radiating to the inner side of the left arm. Don't always feel that there must be relief of pain by nitroglycerin. And, to further complicate the story, persons with pain due to functional heart disturbances or some extracardiac condition occasionally may have pain relieved by nitroglycerin. The pain of spondylitis is often relieved by nitroglycerin. A patient with an anxiety state will have pain on effort.

Although he has a severe anginal syndrome, and despite the fact that his electrocardiogram has become abnormal and he has definite hypertension, this man had a normal resting electrocardiogram shortly before the present illness. I wish to make the point that you must not exclude coronary disease because the physical examination, fluoroscopic study and the electrocardiogram show nothing abnormal. Do a functional test of the heart. A man may have coronary disease even though his resting electrocardiogram is normal.

I have been convinced for many years that our current definitions of hypertension are too low. In the first place, blood pressure rises with age; the average systolic reading for a boy of 20 will be 116, while that for thousands of men of 60 will be 155. Second, if you use one commonly accepted definition of high blood pressure like 160/100 or 150/90, you will find that half the normal population more than 50 years of age have "hypertension." You have to liberalize your definition of hypertension.

Another reason for my belief that current definitions are too low is that many investigators have found that many definitely hypertensive patients (200, 210 or 230 systolic and 110 or even 120 diastolic) live out their normal spans of life and have no complications.

For these three reasons we studied 74,000 persons, gainfully employed, and recorded

their blood pressures. The mathematicians and physicists constructed definitions of what constitutes high blood pressure and what constitutes the normal range for each age group and for both sexes.

In Figure 1 is a frequency distribution curve—not the beautifully symmetric, bell-shaped curve you see in textbooks, but a definitely mathematical one. These are the findings for a group of men 40 to 44 years of age, inclusive. The middle 80 per cent we arbitrarily call "normal"; the extremes of 2.5 per cent at either end (we plotted their blood pressures per age) we call abnormal.

TABLE 1

NORMAL RANGE AND LIMITS OF HYPERTENSION*

AGE	NORMAL RANGE		HYPERTENSION, LOWER LIMIT	
Years	*Male*	*Female*	*Male*	*Female*
		SYSTOLIC		
16	105-135	100-130	145	140
17	105-135	100-130	145	140
18	105-135	100-130	145	140
19	105-140	100-130	150	140
20-24	105-140	100-130	150	140
25-29	108-140	102-130	150	140
30-34	110-145	102-135	155	145
35-39	110-145	105-140	160	150
40-44	110-150	105-150	165	165
45-49	110-155	105-155	170	175
50-54	115-160	110-165	175	180
55-59	115-165	110-170	180	185
60-64	115-170	115-175	190	190
		DIASTOLIC		
16	60-86	60-85	90	90
17	60-86	60-85	90	90
18	60-86	60-85	90	90
19	60-88	60-85	95	90
20-24	62-88	60-85	95	90
25-29	65-90	60-86	96	92
30-34	68-92	60-88	98	95
35-39	68-92	65-90	100	98
40-44	70-94	65-92	100	100
45-49	70-96	65-96	104	105
50-54	70-98	70-100	106	108
55-59	70-98	70-100	108	108
60-64	70-100	70-100	110	110

*From the *Bulletin of the New York Academy of Medicine*, vol. 27, pp. 452-465, July 1951.

Table 1 gives the blood pressure limits developed for us by the mathematicians. Take as an example a man 60 to 64 years of age. His normal systolic range is usually 115 to 170 mm. of mercury. We won't call it abnormal until the systolic pressure reaches 190. In between we call the readings "borderline." You must determine clinically whether such a borderline patient has hypertension. The point is that he may have a systolic reading of 170 and be perfectly normal. On the other hand, if he has a blood pressure reading of 190 or more systolic, you have to call it hypertension.

Let's consider the diastolic blood pressure limits for a man of 58. His diastolic pressure may normally be 70 to 98. A man of 58 or a woman of 58 may normally have a diastolic pressure of 98 or even 100 and still be normal. On the other hand, when a man's or woman's diastolic blood pressure reaches 108, we feel it is definitely hypertension. In between these limits, of course, you use your clinical judgment.

We have used these figures for a few years, and they have been of great clinical value.

We believe that the association of hypertension and diabetes and the relation of hypertension to coronary occlusion have to be re-examined. We have reinvestigated these and found that women with coronary occlusion still have hypertension, even with these higher definitions. But, using these limits, we found that men with coronary occlusion don't have hypertension—at least three-fourths of them don't.

I hope the new table of blood pressure limits will dispel the hypertension phobia. I must warn you not to use the figures too literally. You still must depend on the history, on the enlargement of the heart, on the electrocardiogram, and so on. I repeat, if a 50 year old man has a systolic pressure of 150, I would call it hypertension if the described roentgenographic and electrocardiographic changes are present. But if that man has a blood pressure of 160 or 165 or even 170 and no other abnormal findings can be detected by the methods noted, I would call it normal blood pressure.

Summary

The diagnosis of hypertensive heart disease is made on the basis of an anginal syndrome, an abnormal electrocardiogram, cardiac enlargement or retinal changes. This is particularly true if the heart is enlarged with concentric hypertrophy of the left ventricle, tortuous, dense aorta, and prominence of the aortic knob, or if the electrocardiogram demonstrates high voltage, extreme left axis deviation, RS-T depression and T wave inversion in lead 1. There may be other subjective or objective evidence of heart disease, such as pain in the chest, shortness of breath or signs of heart failure. Coronary artery disease is accelerated by high blood pressure.

If these findings are present, whether a patient be 40 or 60 years of age, whether the blood pressure be 140/90 or 240/140, the diagnosis is hypertensive heart disease. If there are no objective findings or no symptoms, but the blood pressure is 180 to 250 mm. systolic, the diastolic 110 to 160, "hypertension" is the diagnosis. However, there are thousands of people who have no heart disease and who do not have truly high blood pressures, but who are labelled "hypertensive." There is a blood pressure phobia.

What is high blood pressure? Various criteria are used: 140/90, 150/90, 150/96, 150/100, 160/100 and even 180/110.

Blood pressure readings were obtained in 74,000 unselected persons working regularly.

Utilizing the new definitions it was found that the majority of men have normal blood pressure—more than 70 per cent, whereas, even employing the newer and higher definitions of hypertension, more than 70 per cent of the women had hypertension before their coronary occlusion. Hence, in men hypertension is of little importance, whereas in women it is of major importance in the onset of coronary occlusion.

Just as dependence for diagnosis on a single observation or test may be dangerous practice in clinical medicine, so the evaluation of the blood pressure reading is unsound without correlation with the entire examination of the patient.

Recent Developments in the Management of Peptic Ulcer

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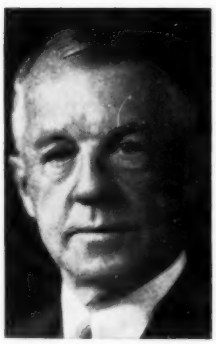
Subjects discussed in this article include indications for surgery in cases of bleeding ulcer, drugs in medical management, the present status of vagotomy, surgery in pyloric obstruction, relationship of hiatus hernia to peptic ulcer, incidence of malignancy in gastric ulcer, and the dumping syndrome.



FRANK H. LAHEY

THIS subject is quite a large undertaking, but I would like to try to answer some of the following questions:

1. When is surgery indicated in a case of bleeding ulcer?
2. How prevalent is the dumping syndrome, what causes it and how can it be avoided?
3. Is the Hofmeister operation satisfactory, and in what manner have we employed it?
4. What is the place of BANTHINE® today in terms of the suggestion that it might abolish surgery?
5. Where does vagotomy stand today, and what is its place in relation to subtotal gastrectomy?
6. What is the incidence of gastric ulcer, what is its relation to malignancy and what is the preferred form of treatment?
7. Under what circumstances should we advise surgery in pyloric obstruction?

There is a real place for the medical treatment of duodenal ulcer and perhaps also of gastric ulcer, with certain reservations and restrictions. We have now treated 16,000 peptic ulcer patients under hospital management. We have operated on only 10 per cent of these, but I think that should be explained. The incidence of surgery in patients with peptic ulcer will be related directly to the adequacy of the facilities for medical management. If there is a good gastroenterologic department, many more patients will be managed medically; otherwise the decision to perform surgery is made earlier. On the other hand we have had to modify the attitude of our own gastroenterologic department—and I think we should modify it still further—so that patients are sent to surgery earlier, particularly those with recurring duodenal ulcer, and so that they are more critical of gastric ulcers with regard to possible malignancy.

The mortality rate for subtotal gastrectomy, which we still think is the operation of choice for most patients with duodenal ulcer, unfortunately is not placed in the proper position. It is not very high; there are enough men today who can do good gastric surgery so that the mortality rate of the operation itself should be relatively low. It is related to the decision as to the type of operation employed once the abdomen is opened and the ulcer visualized,

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palpated and its relationship to the common duct determined—how deeply it is buried in the head of the pancreas and how safely the duodenal stump can be closed. Therein lies the mortality rate for subtotal gastrectomy, particularly for duodenal ulcer. This decision is based on the surgeon's ability to reject subtotal gastrectomy when the ulcer is attached to the bile duct or buried in the head of the pancreas too deeply for safe removal and to substitute for it vagotomy and gastroenterostomy. For this reason I have urged our gastroenterologists not to carry these patients through repeated acute episodes of ulcer activity and of bleeding because bleeding means intractability. Of all patients who have had one hemorrhage, 44 per cent have been medical failures; of all who have had two, 80 per cent have been medical failures. Furthermore, the mortality rate in cases of hemorrhage is real and so we would like to impress our medical and gastroenterologic friends with the fact that they play a not inconsiderable part in the mortality rate of the surgical treatment of duodenal and of gastric ulcer. To them I say, do not carry patients through long periods of medical management, but get them to us earlier, when we can do subtotal gastrectomies or vagotomies and gastroenterostomies, if they seem the proper way to manage the case, with a lower mortality rate.

Banthine as a method of treating duodenal ulcer has been mentioned in many articles and frequently with overenthusiastic statements as to its efficacy. Every once in a while we have a new agent which is going to abolish this, that and the other, including surgery. Banthine is one of these, but today it has gravitated to its proper place; it is just another drug to be used in medical management, particularly for the relief of pain in patients with duodenal ulcer.

Of interest is a report on our own gastroenterologists' experience with 100 selected cases of duodenal ulcer in which the patients were treated with this drug. These cases were selected by Dr. F. E. McDonough on the basis of established records of periodicity of recurrence of symptoms. These patients had had ulcer long enough and we had the patients long enough to know when to expect episodes of distress and discomfort. Of the 100 patients treated with banthine, 59 obtained relief of pain and symptoms did not recur at the expected period of time; 11, because of side effects, had to give up the agent; 30 had recurrences of symptoms. I think everyone today should accept the position that banthine is a good agent for the relief of pain but as to its ability to cure patients with ulcer, it belongs with the alkalis, AMPHOJEL® and the various other medical agents.

It has been most difficult for us to establish an understandable position concerning when to operate on a patient with peptic ulcer because of hemorrhage, but I want to make it very clear that hemorrhage is a much more dangerous complication of peptic ulcer than most people think.

Dr. Lewisohn at Mt. Sinai Hospital collected reports on 3500 cases of hemorrhaging duodenal ulcers from various hospital records and established a mortality rate for medically treated duodenal ulcer of 4.3 per cent. On the other hand, the mortality in 460 surgically treated patients with bleeding duodenal ulcers was 19.5 per cent. That is a startling figure. There is a tremendous number of variable factors that cannot be presented in definite figures as to when to do this and when to do that in patients with bleeding duodenal ulcers. I would like to present one, and that is that the patient who has recurring massive hemorrhage must be brought to surgery on the basis of the skill and experience of the surgeon. Nothing is more hazardous nor is hardly any surgical state associated with a higher mortality rate than that of a bleeding ulcer. Therefore it is my opinion, as has been expressed by Dr. Burrill B. Crohn, that unless an experienced surgeon and good facilities are available, a patient with a massive bleeding duodenal ulcer has a better chance with medical treatment on the whole than with surgery.

Some definite figures and statements are of help in managing this condition. There are two types of hemorrhage. The first is the massive recurring hemorrhage—that is the case for surgery, the ulcer in which massive hemorrhage recurs two or three times. If the patient

is more than 45 or 50 years of age, surgery should be done earlier, if it is to be done. The second type of hemorrhage is that in which the patient has lost 60 per cent of his total blood volume; such a patient is a definite candidate for surgery. The patient with massive hemorrhage whose blood pressure cannot be increased with two transfusions certainly is approaching candidacy for surgery if a surgeon with adequate skill and experience is available.

I would like to leave these rather indefinite statements with one more thought: Never have I seen a surgical state in which such critically ill and hopeless-looking patients could be so successfully operated on and leave the operating table in good condition—if good surgical experience is available. Do not despair of a patient who has bled massively, who is pulseless, who has literally no blood pressure. Once the perforation in the vessel wall is closed and blood is given, such patients have a tremendous capacity to regain their blood pressure and to survive.

There are two or three examples which I think will impress you in this respect. The important one is: Think of what can be done today with patients under anesthesia with artificially produced low blood pressure. Patients with practically no blood pressure can be operated on today and still oxygenation of their cerebral centers is adequate to maintain life and intellect once blood volume is restored and pressures brought up. Think what goes on with cardiac arrest. It takes only a moderate amount of oxygen-laden red cells to maintain the activity of the cerebral centers. Adequate circulation can be maintained to retain mental cerebration merely with manual compression of the heart and alternate distention of the lungs, and deterioration will not occur even if this artificial circulation is maintained for half an hour or longer. We have reported a case of cardiac arrest which occurred with the chest open, so we are sure this is a true statement. In this case there was no spontaneous cardiac action for 22 minutes; circulation was maintained by squeezing the heart and alternately filling the lungs. Cardiac action was completely regained with no cerebral damage, and an electroencephalogram was normal.

Anoxia produces two types of cerebral and liver damage and also damage to other vital centers: (1) the type associated with shock and (2) the type which results entirely from actual loss of blood volume. Therefore I would again urge that even though patients have bled massively and have attained apparently desperate states, an attempt should be made to stop the hemorrhage, with the distinct possibility that these patients can be saved.

Not everyone agrees with our position on vagotomy, but these are the figures that many of you may not have had the opportunity to follow, taken from the report of the Vagotomy Committee published in the book by Dr. D. J. Sandweiss. You can make your own decisions as to the results. This is the follow-up study of 1300 cases that were selected on the basis of experience on the part of the surgeon and good follow-up records.

With gastric resection, we can expect 95.6 per cent of patients with duodenal ulcer without previous hemorrhages to be clinically free of symptoms; with gastric resection plus vagotomy the figure is 96 per cent; with gastroenterostomy plus vagotomy, 71.7 per cent. In duodenal ulcer patients with previous hemorrhages, 96 per cent will be symptom-free with gastric resection alone; gastric resection plus vagotomy, 96 per cent; gastroenterostomy plus vagotomy, 83 per cent.

Vagotomy was supposed to be most effective in gastrojejunal ulcer. It is to be noted in this respect, according to the combined criteria of this report, that in patients without hemorrhages, vagotomy alone gave good results in only 59 per cent, and gastric resection in 81.4 per cent. In patients with previous hemorrhages, vagotomy alone gave good results in 61 per cent, and gastric resection in 86 per cent.

The most valuable data in this report have to do with relief in terms of height of resection and also with comparison of vagotomy plus subtotal gastrectomy with gastrectomy alone. In patients without previous hemorrhages in whom less than 70 per cent of the stomach was resected, 6.3 per cent had postoperative hemorrhages; when more than 70

per cent was resected, only 1.3 per cent had postoperative hemorrhages; with gastroenterostomy plus vagotomy, 2.1 per cent had postoperative hemorrhages. In patients with previous hemorrhages in whom less than 70 per cent of the stomach was resected, 10.7 per cent had postoperative hemorrhages; when more than 70 per cent was resected, only 4 per cent had postoperative hemorrhages; with gastroenterostomy plus vagotomy 6.5 per cent had postoperative hemorrhages.

In a good subtotal gastrectomy about four-fifths of the stomach is removed. The percentage of recurrence is high when less is removed. The Hofmeister resection, with the proximal loop anastomosed to the greater curvature and with an angulating stitch as the last stitch placed to buttress the jejunum over the upper closed end of the stomach, has been the best type of resection for duodenal ulcer in our hands.

I am particularly anxious to speak of the relationship of hiatus hernia to peptic ulcer. With more and more transthoracic gastric resections and total gastrectomies being done, we are learning a great deal more about the effects of high gastric acid on the esophageal mucosa or on the cardiac gastric mucosa when the first portion of the stomach beneath the diaphragm is trapped in a hiatus hernia. In small hiatus hernias many of the symptoms are related more to ulceration or irritation of the lower end of the esophagus or of the sac of gastric mucosa which is trapped in the hernia than to the trapping or hernia itself. For this reason we are becoming more aware of how necessary it is in patients with hiatus hernias to keep gastric acids low and neutralized in an effort to avoid ulceration or esophagitis of the lower end of the esophagus or of this trapped section of gastric mucosa. We are recognizing the undesirable effects of high gastric acids bathing the esophagus, in the production of an esophagitis which eventually can be of the cicatrizing type.

In relation to this, over the past years we have all been aware of the disastrous consequences when a patient with a full stomach is given general anesthesia and of the effects of inspissation of food into the bronchi as a result of vomiting. It is now more clearly appreciated that, as the anesthetists have demonstrated, it is not so much the effect of the food acting as a foreign body on the bronchi as the effect of the highly concentrated hydrochloric acid on the alveolar epithelium, producing edema and pneumonitis. These secondary effects which formerly we did not appreciate were really largely more those caused by hydrochloric acid on alveolar epithelium than the foreign body effect of the inspissated food.

I have often discussed the difficulties of deciding when to operate on patients with varying degrees of pyloric obstruction. There is no difficulty in settling the need for surgery in a patient with long-standing and progressively increasing cicatricial obstruction, but in those with obstruction of varying degrees with active ulcers this is more difficult.

Dr. S. Allen Wilkinson, in this clinic, has aided greatly in this decision. These patients with uncertain degrees of pyloric obstruction are confined to bed throughout the 24 hours for three days, a Levin tube is inserted into their stomachs, and daily residual determinations are made. Information obtained from such a program is of great value in settling whether or not immediate operation is necessary for pyloric obstruction.

These patients are put to bed, an indwelling Levin tube is inserted, and a 3 oz. mixture of malted milk is given every hour. The tube is clamped for the first half-hour and drained for the second half-hour, and the quantity drained in 24 hours is measured and recorded. If the amount of residual during the 24 hour period decreases progressively, it is unlikely that the obstruction is other than the temporary one associated with an edematous pylorus and acute ulcer activity. If, on the other hand, the drainage remains elevated during this 24 hour period, it is unlikely that any measure or method of treatment will avoid the eventual need for surgery, which should be instituted.

It is interesting that there is a direct relationship between those patients who have had an ulcer with partial pyloric obstruction for less than three months and those who have had this partial or recurring obstruction for

more than three months. Of the former, 61 per cent have been relieved by medical treatment and only 39 per cent have had recurrences. Of the latter, only 31 per cent were relieved by medical measures and 69 per cent were candidates for surgery, obviously because of infiltration and fibrosis of the long-standing pyloric reaction.

I would like to say a few words regarding the incidence of malignancy in gastric ulcer. Ideally, I would like to resect every gastric ulcer if I could because in a series of 600 patients studied by Dr. Sara M. Jordan and Dr. Frances H. Smith in this clinic, 21 per cent of the ulcers proved to be malignant. In another series studied in this clinic by Dr. Samuel F. Marshall, it was demonstrated that no diagnostic aid in the history as relates to the amount of weight loss, the complication of hemorrhage, obstruction or perforation, or the height of the acidity would aid us in differentiating gastric ulcer from malignancy. We have, in the past, made the same statement as have many others that in our experience every ulcer which we have ever seen on the greater curvature was malignant. We now have to modify that in the light of our greater experience to the statement that in our experience with ulcer patients about 1 out of every 10 ulcers is a gastric ulcer and we have now seen 6 benign ulcers of the greater curvature. Malignancy in ulcers of the greater curvature is so common, however, that we still believe it is dangerous to treat patients with lesions in this location conservatively and we believe all such ulcers should be resected.

Where does this bring us with the problem of gastric ulcer? Which patient should be treated surgically and which should not? Can we treat these patients with gastric ulcers medically, and for how long? What indications should make us change from medical management to subtotal gastrectomy? Theoretically, we should never treat a patient with gastric ulcer medically. Dr. Shields Warren and Dr. William A. Meissner, who have studied the surgical specimens from cases in which gastric ulcers were resected, report that not more than 5 to 6 per cent of them can even be suspected of showing malignant degeneration on an already existing gastric ulcer. The remainder undoubtedly were cancers from the beginning and have shown only peptic erosion of the mucosa on or about a lesion which was malignant from the start. Based on the now quite freely accepted position that the number of true malignant degenerations on a gastric ulcer is very trivial, theoretically no patient with a gastric ulcer should be treated medically. Dr. Marshall has demonstrated that the variation in the percentage of ulcers in which malignancy is found on removal is approximately the same in all series, ranging from 12 to 20 per cent.

It is all very well to talk about operating on every patient with gastric ulcer, but we and most others have found that this is not possible. Many patients will not accept immediate surgery. Some, of course, are not good risks, and in others the height of the lesion is such as to require almost a total gastrectomy. Therefore it may be of value to list the conditions under which we will permit the medical management of a gastric ulcer. We must first tell every patient of the relative hazards of malignancy in gastric ulcers and he must be aware of the risk he is taking. If, under these circumstances, he accepts the responsibility for medical management, it should be continued only with the understanding that roentgenograms be taken every month for three months, then every two months for six months and then every six months for two or three years. Unless this is done, I know of no way to avoid having these patients get away from the gastroenterologist's supervision and return only when the malignancy has reached a state of inoperability. That this is true has been proved more than once in our experience. We have three friends, two surgeons and one excellent internist, who have gastric ulcers but have elected medical management. One has had two recurrences and still accepts medical management. As bad as this sounds, it is not such poor judgment as it might appear. If it is true that only 5 or 6 per cent of the gastric ulcers show malignant degeneration, it can rightly be assumed that if the gastric ulcer has existed long enough to recur twice, the lesion is not a primary malignancy, with pep-

tic ulceration on the malignancy, and it is a relatively safe lesion to continue treating medically.

One of the problems presented has been that the gastric ulcers were so high that either transthoracic or total gastrectomy had to be considered. Only rarely will total gastrectomy be needed in these cases. Occasionally, however, either transthoracic resection or total gastrectomy will be necessary. We have employed total gastrectomy for high gastric ulcer or gastric ulcer suspected of malignancy—largely the latter group of cases—in 13 cases, and the results have been excellent. There has been but 1 death and that was of a patient in whom total gastrectomy was done as an emergency procedure for a perforated gastric ulcer at the point where the esophagus joins the lesser curvature.

It frequently has been said in relation to the employment of total gastrectomy for high gastric ulcer or gastric ulcer suspected of malignancy that these patients are difficult to feed. That is true, but in the 12 cases in which total gastrectomy has been employed, feeding has been satisfactory and the patients have been quite comfortable. It must be remembered that the feeding of a patient with a total gastrectomy is a difficult problem. It means teaching the patient to chew food thoroughly, a minimum of five meals a day in the beginning, and often that the patient must lie down after meals to avoid the type of dumping syndrome which not infrequently goes with this type of operation but which, with time, tends to disappear.

The dumping syndrome is discussed a great deal in the literature, and it is difficult to talk intelligently about this complication because we do not really know its cause. Probably the best explanation has to do with the dumping of large amounts of gastric contents into the jejunum and the hypoglycemia and hyperglycemia associated with it. It also has a mechanical aspect, with symptoms of distress of the type that would be expected with overdistention of the upper jejunum.

We have been interested in the dumping syndrome, and recently selected a series of consecutive recent subtotal gastrectomies done for duodenal ulcer, stressing our interest particularly in the occurrence of the dumping syndrome. There were but 2 patients with dumping syndromes, in 1 of whom the syndrome disappeared within two weeks. We are quite convinced that the use of an angulating stitch, to produce a trap in the Hofmeister resection, as the last stitch employed to buttress the distal loop of jejunum over the closed end of the stomach has much to do with holding food within the stomach, and that the making of smaller and smaller stomas likewise has played a not inconsiderable part in reducing the incidence of this syndrome.

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Spontaneous Cerebral Hemorrhage of Congenital Origin in Pregnancy

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Spontaneous cerebral hemorrhage of congenital origin in normal pregnancy is readily confused with legitimate complications of the parturient state, and must be more common than hitherto suspected. It requires a specific diagnostic and therapeutic approach to effect the full potential fetal and maternal survival.

CHARLES L. SULLIVAN

A PREGNANT woman is as subject to the uncertainties of mortal existence as is her barren sister. This fact is readily forgotten, especially in the light of the ever decreasing mortality rate in pregnancy. This is especially true of the laity, who readily ascribe all deaths during pregnancy as due intrinsically to the pregnant state. Spontaneous cerebral hemorrhage of congenital origin, to the contrary, is an entity reported in 1 per cent of all autopsies, and accounts for 2 per cent of all sudden deaths which occur in the pregnant and the nonpregnant state alike.

Two excellent reviews of the literature describing this condition in otherwise uncomplicated pregnancies recently have been reported by Conley and Rand[1] and Schwartz,[2] who have collected a corrected series of 29 cases. An additional case was reported by the Committee on Maternal Welfare in a study of maternal mortality in Massachusetts during the past three years.[3] Thus, for a total of 31 cases (30 previously reported cases and the 1 reported herein), the maternal and infant mortality rates were 52 and 29 per cent respectively. This is approximately the same maternal mortality rate as that reported for this syndrome in the nonpregnant state.

The following case is presented because the paucity of such reports indicates that the condition must readily be confused with other complications of pregnancy, principally preeclampsia and eclampsia, which require a different therapeutic approach and carry a much lower infant and maternal mortality rate.

Case Report

A 23 year old primigravida was admitted to the hospital in her forty-first week of pregnancy with a history of ruptured membranes of 12 hours' duration and no labor. The prenatal course had been uncomplicated, with no evidence of toxemia. There had been a total weight gain of 18 pounds. The past history was noncontributory, and it is interesting to note that this patient had been a competitive golfer and had won many championships. She

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had been seen by her attending physician on the day prior to admission, at which time her blood pressure was 128/72 and the urine was negative for albumin. She was completely relaxed and without subjective complaint. There was no evidence of labor. Urinalysis revealed no albumin, and the blood pressure on admission was 134/74.

The onset of hemorrhage was sudden and without prodromal symptoms. Within 10 minutes of a primary visit, the attending physician returned to the patient's room and found her writhing about and complaining that she felt as if an ax had been driven into her head. Her skin was cold and clammy, there was slight ptosis of the right eyelid and the right pupil was dilated. The blood pressure was 170/90. On the basis of the normal history and the objective findings, a diagnosis of ruptured cerebral aneurysm of congenital origin was made and a diagnostic lumbar puncture performed. The spinal fluid pressure was 400 and the fluid pink-tinged.

Within five minutes the patient became unconscious, and within a half-hour the blood pressure was 220/100 and a catheter urine specimen showed 4 plus albumin. Within three hours a uric acid determination was 6.5 mg. with a nonprotein nitrogen of 37 mg.

The patient was given oxygen by mask, and 45 minutes after the onset of the hemorrhage there was a sudden cessation of respiration; the pulse remained slow and forceful. She was maintained on artificial respiration until a tracheal catheter could be placed, and thereafter respirations were carried on artificially in a closed circuit.

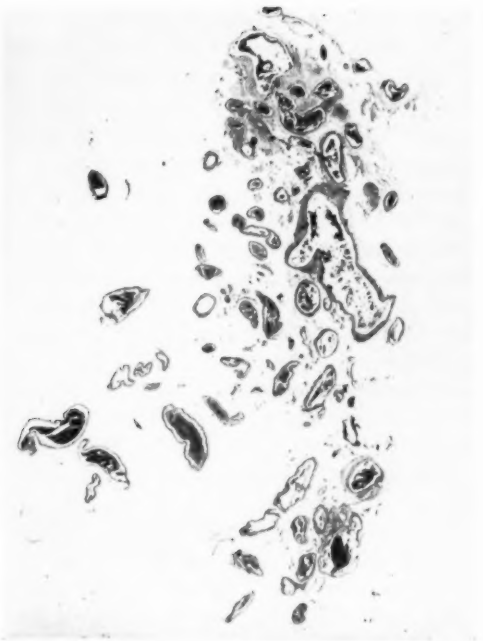
One hour after cessation of respiration the patient's condition began to deteriorate further, with increasing cyanosis and a thready, rapid pulse. The fetal heart rate, which until this time had been around 120, dropped precipitously to 100. With the patient in bed and without anesthesia, a classic cesarean section was performed, and a live male infant in good condition with spontaneous respirations was delivered without event. The skin wound, which had shown no bleeding points on initial incision, required ligature of bright red bleeding points on closure.

After cesarean section was done and for six hours immediately following the procedure there was an immediate and marked improvement in the patient's general condition. The color became normal and the pulse slowed to 80 to 90 and was regular, but the blood pressure remained high. There were no spontaneous respirations. The improvement was so marked that an attempt was made to reduce a possible cerebral pressure cone by intrathecal injection of saline, but without success. The second tap showed bloody spinal fluid.

The patient was placed in a Drinker type respirator and good oxygenation was maintained, as indicated by skin color. There was no notable change in the patient's condition for the next six hours. Then there ensued a state of shock which was neurogenic in origin with many bizarre manifestations. Only fleeting pulse and blood pressure recordings could be made. With the onset of the shock there was moderate and continuous vaginal bleeding from an atonic uterus. Close observation showed that whenever the patient had a discernible pulse or blood pressure there was concomitant good uterine tone and no bleeding. During this phase the uterine hemorrhage was controlled by pressure on the fundus against the symphysis.

The temperatures of the extremities varied; there were areas in which the arrectores pilorum muscles were contracted and others in which they were relaxed. There were no eye signs and both pupils were widely dilated. During this episode the patient received 1400 cc. of whole blood with various vasopressor substances, and this sympathetic fugue finally came to an end with stabilization of a pulse rate of 80 and of good quality and a blood pressure of 90/60 to 100/60.

The general state of the patient remained unchanged for the next 18 hours, at the end of which time there was noted some degree of reactivity to light by the left pupil—the first activity of any sort following the cessation of respiration. The color and peripheral circulation remained good with a pulse rate of 80 to 90 and a blood pressure of 100-110/60-70. Urinary output was adequate, and fluid with caloric content was administered



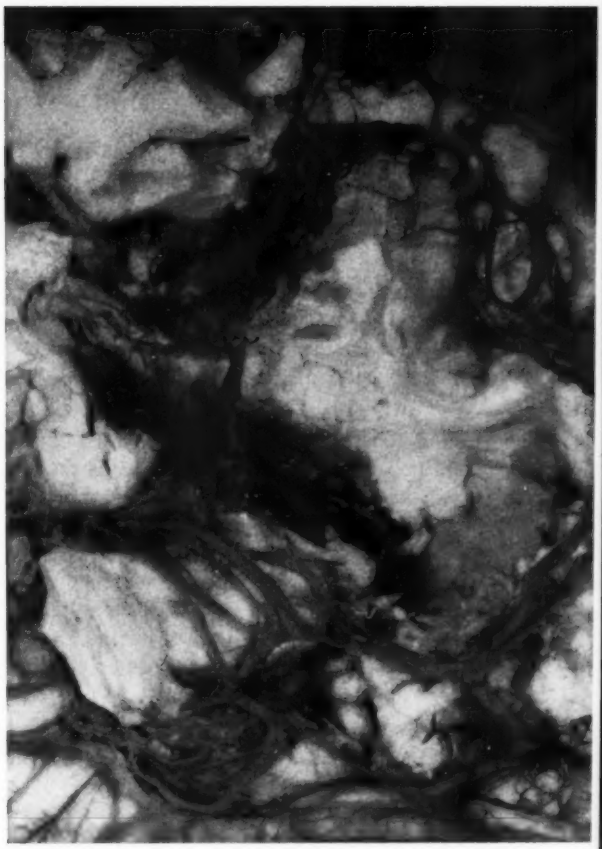


FIGURE 1 *(right)*. Gross: Serpiginous nest of anomalous vessels deep in sylvian fissure (temporal lobe removed).

FIGURE 2 *(above)*. Microscopic: Representative cross section of vascular anomaly containing arterioles and venules.

through a Levin tube with absorption. The eyegrounds, which had been hazy from the onset, now became clear, and the vessels were visible and showed numerous flame hemorrhages. At the end of 45 hours, there was a sudden and complete vascular collapse with death. At no time during this episode was neurosurgical interference considered feasible by the attending neurosurgeon and neurologist. The infant did well and was discharged as a normal newborn at the usual time.

Autopsy (Figures 1 and 2)—The brain was asymmetric, the right side being larger. On reflection of the dura there was noted a large, fresh blood clot in the right subarachnoid space extending over the entire right hemisphere but being most marked along the sylvian fissure. The brain on removal weighed 1,350 gm. A bilateral cerebellar pressure cone and a right temporal pressure cone were evident. There was a linear depressed notch along the left side of the brain stem (so-called Kernohan's notch). Inspection of the vessels at the base of the brain revealed a normal pattern, and all had thin walls and patent lumens. No aneurysmal dilation was seen. In attempting to trace the right middle cerebral artery as it courses along the sylvian fissure,

gentle traction on the right temporal lobe caused a tearing which was found to be due to marked thinning of the brain substance in this lobe caused by a rather firm intracerebral clot measuring roughly 8 by 4 by 3 cm. On removal of the clot, a tangled mass of vessels could be seen resting in the deep recess of the sylvian fissure. The brain was then fixed for further examination.

After fixation, the right middle cerebral artery was dissected free of clot and found to enter a tangled mass of anastomosing vessels. There was a large, thin-walled, collapsed vessel entering the brain substance which coursed over to the vein of Galen. No break was demonstrable in this tangle of vessels, but it appeared that this focus was the only source from which the hemorrhage could have occurred. Microscopic sections of the vessel walls showed moderate amounts of subintimal hyalinization. There was no inflammatory reaction in or about the vessel walls, and thrombi were absent. Elastic tissue stains showed the vascular anomaly to be of arterial and venous origin.

Final diagnosis—Congenital vascular abnormality with spontaneous rupture into subarachnoid space and right temporal lobe.

Discussion

This lethal syndrome, occurring as it did under the observation of the attending physician, was followed constantly for a period of 45 hours and gave an unusual opportunity to observe the manifestations of this condition in pregnancy. It is quite obvious that spontaneous subarachnoid hemorrhage readily can be mistaken for a fulminating eclamptic state, and at times the differentiation may be impossible. The physiopathologic signs and symptoms of spontaneous subarachnoid hemorrhage are exactly the same as those of eclampsia—namely, headache and/or coma and convulsions, albuminuria, hypertension and altered nitrogen metabolism. The one differential point lies in the bloody spinal tap of subarachnoid hemorrhage, the *sine qua non* of this diagnosis and yet, as in the case reported, an interval must elapse between the time of the hemorrhage and the time of the tap or this differentiating point will be lost.

Subarachnoid hemorrhage comprises 7 per cent of all cerebral vascular disease and approximates in frequency the 8 per cent incidence of parenchymal cerebral hemorrhage[4] with the important added fact that it is more common in the younger or pregnancy age group. The immediate physiopathologic changes which occur in an otherwise normal pregnant woman when spontaneous subarachnoid hemorrhage occurs—severe headache, convulsions and/or coma, sensory or motor disturbances, hypertension and albuminuria with derangements of blood chemistry—mimic perfectly a fulminating eclampsia. Cerebral hemorrhage also occurs in 15 to 40 per cent of all cases of eclampsia, as proved by autopsy, and the fact that in many instances the source of the hemorrhage cannot be demonstrated even at autopsy further complicates the clinical picture. Thus, with the rational election of the most probable diagnosis in a pregnant woman in such condition, the true incidence of this syndrome is hard to determine. Magee[5] in a study of 150 cases of spontaneous subarachnoid hemorrhage reported that prodromal headaches occurred in only 18 per cent before hospitalization. When it is recalled that severe recurring headaches occur in 9 per cent of all persons in a cross section of a healthy population,[6] there is little basis for suspecting this syndrome before the cataclysm occurs. The water-retention headaches of pituitary origin in pregnancy further tend to reduce the differential. While it is true that a ruptured aneurysm may simulate eclampsia, it is also true that preeclampsia or eclampsia may mask an underlying and/or concomitant vascular defect.

Certain other conditions may mask this syndrome, namely, the headaches occasionally following the use of either ergot or PITOCIN®, but principally the postspinal headache following low dose intrathecal anesthesia. The patient with a severe or unduly persistent postpartum headache of supposed oxytocic or spinal origin deserves the security of a spinal tap to rule out the presence of this condition. The post-ergot headache is well known, and Sullivan and Heffernan[7] have reported the oc-

currence of severe headache following the use of pitocin. In a personal series of 1000 spinal anesthetics for delivery, along with the usual incidence of spinal headaches 2 patients required diagnostic spinal tap.

Maternal prognosis in pregnancy is readily divided into two groups, those patients with coma and those without coma. This is contrary to what is observed in the nonpregnant state, for Magee[5] stated that the presence of coma only slightly worsens the outlook for the nonpregnant patient, and Wolff[8] observed that many patients with this sign recover and that it is without prognostic value. Of the 31 collected cases of spontaneous cerebral hemorrhage in pregnancy—all without suggestion of toxemia or other factors—the presence or absence of coma was mentioned in 29, and it was present in 20 (15 of 18 prepartum cases, 2 of 3 intrapartum cases and 3 of 8 postpartum cases). Three out of 4 women with coma died, whereas there were no maternal deaths in cases in which this sign was absent. The fact that 2 of the 5 patients who recovered following coma were treated surgically and the additional knowledge that in the acute phase the diagnosis of location can be made by arteriogram[9] make it imperative that this diagnosis be seriously considered in those patients who are thought to have active or impending eclampsia.

The presence or absence of maternal coma is also the dividing line in fetal mortality. Of the 31 collected cases, the outcome for the child was not reported in 4; 7 infants already had been delivered before the onset of the hemorrhage, and 3 fetuses were nonviable. Of the 17 alive and within the uterus at the time of the cerebral disaster, 12 (70 per cent) survived. Maternal coma was present in 13 cases, and 5 of these babies died. Without maternal coma there were no fetal deaths, for the 5 infant deaths occurred in cases in which the comatose mothers did not have time to deliver their infants from below before they themselves succumbed. Of the 12 babies salvaged, 7 were delivered by cesarean section. Of the 7, 5 had mothers in coma. Five were delivered from below, and 3 of these 5 mothers were in coma at the time. Thus with maternal coma only 3 out of a possible 8 babies were saved while waiting for the patient to deliver from below, whereas section would have subjected these babies to no greater risk than is normally inherent in the elective section. Of the noncomatose mothers, 2 babies were delivered by section and 2 from below.

That spontaneous cerebral hemorrhage in the mother has no direct effect on the fetus is obvious, and no viable fetus died if the mother had time before her own death to present her offspring to the world through the natural channel. Thus it is evident that the time element is important in delivery from the standpoint of the baby, and that cesarean section of extrinsic indication is mandatory when it becomes obvious that a woman with this syndrome shows signs of deteriorating.

The term "extrinsic" is used to delineate these sections from those of purely, or intrinsic, obstetric origin. A cesarean section of extrinsic indication in a mother approaching a moribund state is laudatory when it is realized that such a procedure also benefits the maternal partnership by allowing greater maternal aeration due to less splinting and greater excursion of the diaphragm as well as by alleviating the strain of the placental shunt, as was well demonstrated in the case reported. Maternal oxygenation is markedly improved also, due to the withdrawal of the well known avidity of the fetus for oxygen. We have recently seen this improvement-phenomenon occur in a moribund patient whose pregnancy was complicated by an acute surgical emergency.

It is admitted that such procedures are not helpful to cesarean section statistics and that to determine the proper time to intervene requires care and judgment, the lack of which could easily lead to abuse. It will also help to perpetuate the canard that it is possible to sacrifice the life of the mother in the interest of the child. In this series postmortem section was attempted in 3 instances without return of a viable baby.

The attempt to salvage the life of a baby after the death of its mother is salutary in design, but this highly dramatic situation is paralleled only by the futility of the his-

trionics involved. The gradual death of the maternal organism is followed so closely by irreversible changes to and the morbid decline of the unborn that in all medical literature there have been reported less than 100 successful postmortem sections.[10] Therefore it is only rational to perform a section of extrinsic indication in the presence of a lethal maternal state *before*, and not *after*, the inevitable deteriorating maternal condition has produced an overwhelming condition of fetal anoxia or one sufficient to jeopardize the right of the unborn to life.

Of the total of 31 cases collected, 19 occurred prepartum, 3 intrapartum and 9 postpartum. Sands[11] and Symonds[12] have shown that women with congenital vascular anomalies can stand the strain of multiple sequential pregnancies without untoward event, only to have a spontaneous hemorrhage in a subsequent pregnancy or years later without conception. Ninety per cent of Magee's[5] patients were at rest when the hemorrhage occurred.

It is noteworthy that 70 per cent of the hemorrhages in pregnancy occurred from the thirty-sixth week through the immediate postpartum period. Just why this high percentage of all reported cases should be concentrated in one-tenth the duration of pregnancy is not clear. It may be postulated that the sudden decline of hormonal influences, affecting blood vessel tone, blood volume and cardiac output, are precipitous at this time in contrast to their previous gradual build-up. It could be that the anomalous vessels are able to accommodate the gradual influences of pregnancy for a period of 36 weeks but, coincidental to the aging of the placenta, succumb to the reversal of this process in the short span of a month.

Pregnancy in a woman with a known vascular anomaly should be terminated by cesarean section as soon after the thirty-sixth week as the size of the infant indicates viability, both in maternal and in fetal interest. This is especially true when it is recalled that the over-all incidence of coma in pregnancy with this syndrome is 66 per cent, but that this incidence increases to 86 per cent starting at 36 weeks and continuing through the intrapartum state, carrying with it a 75 per cent maternal mortality rate. Oxytocics should not be used post partum if they can be avoided.

Conclusions

1. Spontaneous subarachnoid hemorrhage simulating the syndrome of eclampsia is undoubtedly masked by the latter as often as it assumes the confuser's role.

2. All patients with eclampsia, especially those whose condition is described as fulminating, as well as those patients with severe spinal or oxytocic headaches, require differential diagnosis by means of a diagnostic tap and/or arteriograms to rule out subarachnoid hemorrhage.

3. The over-all mortality rates for mother and infant are 52 and 29 per cent respectively, but rise precipitously when maternal coma supervenes.

4. With the onset of coma or in the presence of a deteriorating neurologic state, delivery by cesarean section is mandatory on the basis of the time element. Postmortem section should not be planned in preference to antemortem surgery.

5. Women with known vascular anomalies should be delivered by section as soon after the thirty-sixth week of gestation as the size of the fetus indicates, in the interest of maternal and infant safety.

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GENERAL PRACTICE *Review*

This department offers the latest, proved methods for the treatment and management of commonly encountered conditions based on the extensive experience of the physicians who prepare these summaries for POSTGRADUATE MEDICINE.

The Treatment of Peripheral Vascular Diseases
I. Arterial Diseases

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THE diseases of the peripheral vascular system consist chiefly of disorders of the arterial, venous and lymphatic pathways in the limbs. The most important arterial diseases are (1) peripheral arteriosclerosis, which may or may not be associated with diabetes mellitus, (2) thromboangiitis obliterans, (3) Raynaud's disease, (4) peripheral embolism and (5) aneurysm, either luetic or arteriosclerotic.

Peripheral Arteriosclerosis

The treatment of peripheral arteriosclerosis in the majority of patients, when the disease is recognized before actual gangrene of the foot or toes has developed, should consist of an adequate lumbar sympathectomy with removal of at least the first, second and third lumbar ganglions. Sympathectomy does not yield as good results in the majority of diabetic patients as in the nondiabetic, because of their age and the frequently associated peripheral neuritis, so selection of cases is very important. It is believed, however, that a patient with diabetic peripheral arteriosclerosis seen in the fourth or fifth decade of life probably will benefit from a lumbar sympathectomy.

This form of therapy unfortunately does not relieve the symptoms of intermittent claudication in the majority of cases. For that reason the newer procedure of attempting to restore arterial continuity, if there is an area of segmental occlusion in either the iliac or the femoral arteries, should be tried. This procedure consists of excising the occluded area and restoring the continuity either by a homologous arterial graft or preferably by an autogenous venous graft. Arteriography must be performed to determine the site of occlusion of these major arteries.

Many patients are too old for surgery of either of these types, and for that reason the time-honored postural exercises should be prescribed. These consist of a short period of elevation, never longer than a minute, to drain the blood out of the limb; a period of dependency, usually from 3 to 4 minutes, to

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allow blood to make its way down into the distal part of the limb, and then a period of rest in the horizontal position for 5 minutes. This 10 minute cycle should be repeated at least 6 times in succession, and the whole series carried out 2 or 3 times a day, making a total of 3 hours of exercise a day. In many cases, arterial collateral circulation will improve under these conservative measures, and the method is invaluable for the aged.

In the majority of cases in which gangrene of the foot develops, some type of major amputation—of the lower leg or in most cases preferably above the knee joint in order to obtain satisfactory healing—should be done after it has been determined that the other methods of treatment directed toward saving the limb will not succeed.

Thromboangiitis Obliterans

The preferred treatment of thromboangiitis obliterans is lumbar sympathectomy, since this disease occurs in the relatively younger age group in whom vasomotor activity is still present and active. It is imperative, however, that these patients stop smoking completely in order to get the best results. In some instances the use of the anticoagulant DICUMAROL® over prolonged periods may be of help, especially in early cases in which the chief evidence of disease is a migratory type of superficial phlebitis.

Raynaud's Disease

This is a disease primarily of the arterioles and capillaries. The major arteries as a rule are not involved. The upper extremities are most frequently affected but in some cases the lower extremities are involved. An increased activity of the vasomotor sympathetic system can be demonstrated, and for that reason an adequate sympathectomy is the method of choice in severe cases. In milder cases the sympathicolytic drugs, such as PRISCOLINE® or RONIACOL®, may be used with some benefit. If sympathectomy is performed for the upper extremity it should be a radical sympathetic ganglionectomy, including removal of the inferior cervical and the upper 3 or 4 dorsal sympathetic ganglions, and in addition the second and third spinal nerves with their intraspinous roots. Even with adequate sympathetic neurectomy a complete cure cannot as a rule be obtained, because in most instances these patients have an increased sensitivity to cold and thus should be warned to protect their hands and fingers during the winter months.

Peripheral Embolism

This disease usually originates as a result of the lodgment of a blood clot arising from the left auricle of the heart, or in some cases from the left ventricle following coronary thrombosis in one of the major blood vessels. It is one of the few real surgical emergencies, because if adequate treatment is delayed more than 8 to 10 hours, many limbs may be lost. The treatment of choice is an embolectomy by direct exposure of the site of embolism, even the bifurcation of the aorta, with removal of the blood clot. In the majority of patients this can be done with brilliant results and complete restoration of the circulation in the limbs. For patients who are too ill to undergo this procedure, it is recommended that the anticoagulants heparin and Dicumarol be used to prevent formation of a secondary thrombus distal to the site of embolism. Intermittent venous occlusion will also help augment the circulation distal to the site of embolism, with the prevention of gangrene. As is the case with surgical embolectomy, the more conservative medical measures must be carried out at the earliest possible time after embolism to prevent the formation of the secondary distal thrombus which, if formed, in the majority of cases results in gangrene of the extremity.

Aneurysm

Aneurysms may be of luetic or arteriosclerotic origin. The former are becoming rarer due to control of the primary disease, syphilis, whereas arteriosclerotic aneurysms are becoming more prevalent due to the increase in the life span. The method of intrasacular wiring—passing hundreds of feet of wire into the aneurysm—is useful in many of the thoracic types, which as a rule are luetic in origin. This method also has been used for

aneurysms of the abdominal aorta, but with the recent advances in vascular surgery it is now believed that in some cases an aneurysm of the abdominal aorta may be resected and replaced by a homologous aortic graft. Aneurysms frequently arise also in the popliteal artery. These should be removed in all cases, because if they are not, gangrene of the extremity usually results and may lead to a fatal outcome. The method of treatment that is recommended is a preliminary lumbar sympathectomy followed by an aneurysmectomy within 2 weeks. In suitable cases restoration of the continuity of the arterial tree by means of an autogenous venous graft may be done with benefit.

The Problem of Diarrhea

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THE purpose of this discussion is not to encompass all phases of the subject of diarrhea but rather to emphasize some factors of practical importance in the management of this problem.

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The acute epidemic diarrheas which are self-limited will be excluded from consideration. The most frequently encountered chronic diarrheas are of functional origin. The chief contributing factor may be neurogenic or nutritional but most often is a combination of these elements. Next in frequency are the diarrheas due to ulcerative or cicatrizing disease of the small and large bowel. Cicatrizing disease, formerly considered to be limited to the terminal portion of the small intestine, has been recognized to include increasingly larger areas of the gastrointestinal tract—namely, the colon, stomach[1] and perhaps the esophagus.[2]

In a busy clinic practice we have become accustomed to seeing relatively large numbers of patients with neoplasm, particularly carcinoma of the colon or stomach and less often of the small intestine, causing intermittent diarrhea. As a consequence of the radical surgery required to effect a cure, or palliation, the internist is often asked to manage problems of defective absorption, disordered motility, and rapid transit of nutritional elements. It is wise under these circumstances to explain in terms of the patient's understanding the pathologic physiology and corrective surgery involved in such illnesses. For example, if a patient on whom a right hemicolectomy has been performed for advanced cicatrizing enteritis is apprised of the water-absorbing function of the removed segment of his intestinal tract, he will better understand and accommodate himself to experiencing 4 to 8 loose dejections daily. Further encouragement can be offered these individuals by indicating the possibility of future tendencies toward more normal frequency and consistency of dejections.

While bacterial and parasitic agents are not generally the cause of chronic diarrhea, they must always be considered, and when the possibility exists of their presence as etiologic factors, proper investigation should be instituted. Fresh warm stool specimens submitted for culture usually identify the dysentery bacillus in the early, acute phase of this illness.

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The agglutination tests are of little practical value inasmuch as they do not become positive until the disease has been well established. Amebiasis and taeniasis are not uncommonly encountered as causes for diarrhea. Proper analysis of fresh warm stool specimens with the identification of the cysts or trophozoites of the amebas and the visualization of the characteristic ova of intestinal parasites or motile proglottides of the beef tapeworm are pathognomonic of these illnesses.

Adequate fecal analysis will assist materially in disclosing defects in enzyme function by the disclosure of undigested or poorly digested meat fibers, neutral fat and fatty acid crystals. These findings may reflect poor intestinal enzymatic function due to faulty absorption as in the sprue syndrome or in some instances of primary pancreatic disease. Diverticulosis coli, present in 10 per cent of the adult population,[3] is not important as a cause of diarrhea except when inflammation is superimposed. Great care must then be exercised in some of the more obscure cases to exclude carcinoma, a problem which may test one's diagnostic acumen to the depths and which, as a matter of fact, may not be settled until surgery has been undertaken.

Tuberculosis of the alimentary tract likewise is uncommon but can be identified most often in the ileocecal region radiologically and may be confused with cicatrizing enterocolitis. Characteristic cultures and guinea pig tests and sometimes associated chest disease may be helpful in establishing the diagnosis.

When pain appears intermittently in conjunction with diarrhea, thought should be given to the possibility of a partially obstructing lesion due to adhesions occurring subsequent to multiple intra-abdominal surgery, diverticulitis, neoplasm (carcinoma, leiomyoma, polyps), colitis, enteritis, intussusception, and so forth. One should not neglect the possibility also of mesenteric thrombosis with infarction[4] occurring in the middle or older age group when these symptoms occur.

Helpful Objective Information

When the history has been gleaned, one of the first observations should be to look for evidences of shock—dehydration, perspiration, falling blood pressure, weak and perhaps rapid pulse, and fever. Rapid determination of depleted blood levels and electrolyte factors with correction of these factors by transfusions and infusions to physiologic levels may be lifesaving. The location of pain and the presence of a mass, particularly in the right lower abdominal quadrant, are highly suggestive of cicatrizing enteritis, so frequently mistaken for acute perforating appendicitis although the latter, or neoplasm, under these circumstances, should be increasingly suspected past middle age. A rope-like or sausage-shaped mass in the left lower abdominal quadrant is characteristic of a spastic and hypertonic descending or sigmoid colon, and also of diverticulitis.

While diarrhea in an obese patient often connotes a benign etiology, one must be alert to the possibility of preceding weight loss due to an organic lesion. Therefore, while current weight levels are important, they are not nearly so informative per se as a comparative analysis with weight values for 6 and 12 months preceding the onset of illness.

The sigmoidoscope should be employed as a diagnostic aid in all instances of diarrhea because of the prevalence of rectal or lower colonic neoplastic or inflammatory causes for this symptom. No one can estimate the untold number of tragedies which have resulted from the failure of the physician to perform adequate digital and sigmoidoscopic examinations in relation to this problem. Equally important in judging the condition of the mucous membrane is the determination of the physical and chemical state of fecal content. In addition to inspecting the fecal specimens for evidences of defective enzyme function and parasitic factors, a fresh warm specimen submitted for culture will result in the detection of pathogenic enterogens if they are present. Further examination may reveal microscopic evidence of blood and exudate. This latter phase of the examination may be unrevealing when variable degrees of decomposition of free blood in the alimentary tract have occurred, thus obscuring microscopic evidence of blood. The guaiac test has been very

reliable in our hands for the determination of the chemical presence of a significant degree of occult bleeding. The toluidine and benzidine tests are too sensitive to be of practical aid. Careful inspection of the anal and perianal tissues for evidences of fissures or fistulous tracts may reveal contributory causes or provide a clue as to the principal cause of diarrhea.

If the diarrhea is in the active phase there need be no fear in beginning the radiographic study with a barium swallow and motility series in order to determine the rapidity of transit, character of motility, or presence and degree of organic involvement. If, on the other hand, there is any doubt as to the presence of obstruction, the barium enema should precede the upper gastrointestinal series. In the latter instance preparation with a purgative is contraindicated. A cleansing enema is usually satisfactory under these circumstances. Inspissated barium accumulating above an obstructing colonic lesion and resulting from injudicious barium examination of the upper gastrointestinal tract may not only be difficult to extract but also constitute a serious complication requiring emergency surgical intervention. Occasionally the cause for loose dejections with bleeding escapes the examiner until a barium air contrast enema has been performed and a polypoid lesion or polyps are discovered. In performing this examination special views should be taken of the rectosigmoidal area for it is here that a neoplasm may be hidden. Before introducing any barium into the digestive tract it is desirable to obtain a scout film of the abdomen. If obstruction is suspected, a lateral film in the horizontal position and an upright film are indicated. In this manner the presence or absence of gas-filled loops and fluid levels and their distribution can be quickly determined, thus helping in the decision as to the next step in the radiographic examination. It is routine to obtain an x-ray of the chest to exclude a pulmonary cause for diarrhea.

Some Therapeutic Considerations

Whatever the cause, the first step in attempting to correct the diarrhea should be to enforce rest, of the digestive tract and of the entire body. For example, in the medical management of the active phases of cicatrizing enteritis or ulcerative colitis it is becoming customary to prescribe long periods of bed rest much as has been the manner for patients with pulmonary tuberculosis. The rationale for this approach stems from knowledge of the nonspecificity of these illnesses. This measure facilitates building up the body defenses and nutritional levels in order to bring about desired healing. The period of rest to be recommended must be adjusted to individual needs and may vary from a short period of hospitalization to several months of rest at home or in an appropriate sanatorium.

The second objective in the management of diarrhea is the maintenance of a satisfactory nutritional balance. This entails not only fluid equilibrium but also careful and as frequent determinations of electrolytic and protein factors as are necessary. It has been established and is well known that a negative nitrogen balance appears early even in minimal ulcerative colitis. Therefore it becomes imperative to rectify this deficit with adequate protein supplement, preferably orally and certainly by the parenteral route should the patient be too ill for oral alimentation. The serum albumin fraction is of great help in the total assay of liver function and protein stores. Human albumin may be given intravenously in 100 ml. quantities daily for 7 to 10 days when correcting for protein deficits. In many instances such procedures may reverse a critical situation. Severe malnutrition as a result of protracted diarrhea is often associated with anemia which may be masked by dehydration and concentration of blood volume, but here clinical judgment is of utmost importance and the most satisfactory replacement measure is the whole blood transfusion. In less critical situations, anemia due to blood loss, although minimal, may not be corrected by other therapeutic measures. On these occasions immediate and rapid progress may originate from a single blood transfusion.

Particular importance should be given to the serum chloride, potassium, calcium, phosphorus and carbon dioxide-combining power

levels. These determinations should be made as often as the clinical condition of the patient warrants. Serum potassium levels now can be obtained rather easily in a few minutes with the aid of the flame photometer, and in some instances the potassium concentration is indicated by the character of the T wave deflections in the electrocardiogram. Potassium deficits may be roughly in proportion to the severity of the diarrhea. During potassium deficiency, in addition to prescribing potassium chloride by mouth, 1 or 2 ampules (20 to 40 mEq.) of potassium chloride should be added to intravenous infusions when laboratory and clinical data point to this need.

The type of infusion solution to be selected will be determined by the presence of simple dehydration, or dehydration with alkalosis, acidosis, hypoproteinemia, or imbalance in other electrolyte components. Physiologic saline, 2 per cent saline, Ringer's or lactated Ringer's solution, and sixth-molar lactate solution may be selected in appropriate instances. Solutions of 10 per cent glucose concentrations and the amino acid mixtures add to the caloric value, although 10 per cent invert sugar may be more rapidly administered and efficiently utilized than the simple glucose preparations. Calcium gluconate may be indicated intravenously or intramuscularly. Due to impaired motility and absorption, vitamin factors are deficient and these should be replaced in parenteral fluids whenever possible. Likewise, it is our opinion that vitamin B complex and crude liver extract in 2 cc. and 5 cc. quantities respectively may be given with merit intramuscularly, alternatively daily or less frequently as the situation improves.

Difficult problems of fluid and electrolyte imbalance may be encountered in severe disturbances of motility. This infrequently occurs on occasions when an ileostomy is performed. Such may be the case also when the total small intestinal absorbing surface has been reduced to a critical level due to a high enterostomy which has been performed as a lifesaving measure because of extensive disease of the small intestine or enterocolonic disease. Here the equipment described by Scribner[5] for rapid analysis of electrolytes collected from the excreta (ileostomy drainage and urinary tract) provides the physician with information necessary to make rapid adjustments in therapy when needed.

Other measures in the general management of severe diarrheas should include paregoric in teaspoonful quantities, or deodorized tincture of opium, sometimes better tolerated by the patient in 10 minim doses every 4 hours, if necessary, day and night. Preparations containing such inert substances as bismuth and kaolin may be given orally to advantage. Peristaltic inhibition may also be assisted by using antispasmodic and sedative preparations such as atropine and the barbiturates and their derivatives. In some instances the anticholinergic drugs are of help. These drugs should be administered parenterally for best results when the oral route is not practical.

Since this is a general discussion of the subject of diarrhea, no attempt at classification of the various etiologies has been made. However, in passing, when specific bacterial or parasitic agents are encountered, the specific antidote should be quickly employed and in adequate quantities. These aids include the antibiotics, sulfonamides, amebicides, and so forth. Local applications of NISULFAZOLE® or olive oil in the form of retention enemas may facilitate healing in some instances of nonspecific proctitis. Precautions should be taken so as not to aggravate the diarrhea by administering any of these drugs injudiciously.

An observation of interest is that there seems to be less enthusiasm for the emulsifying agents such as TWEEN 80® and allied substances in the sprue syndrome or in conditions in which there is impairment in fat emulsification, and thus impaired absorption. In some of these conditions the difficulty appears to center in a disordered small intestinal motility, thus interfering with the emulsification and absorption patterns. The major approach then is to attempt to improve the motility pattern. When the pancreas has been proved defective in its fat-splitting or multiple enzyme functions, large doses of pancreatin, in the order of 30 to 50 gr. 3 times daily, have been employed with resultant improvement in some cases.

Finally, a discussion of diarrhea should include at least an allusion to dietary management, and here it is possible to apply, in general, similar principles in all forms of diarrhea. If the illness is too critical or too acute to permit oral alimentation, the parenteral route must be utilized to sustain a caloric balance as nearly as possible. Oral feedings should begin as soon as the patient can accept nourishment by this route. The quality, quantity and frequency of caloric intake will be determined by the clinical course of the illness.

At first the diet should consist of soft solids including eggs (poached, scrambled in the top of a double boiler, or coddled), macaroni, spaghetti, custards, junkets, JELL-O®, gelatins, SALTINES®, white cooked cereals, clear broths and dry toast. Feedings should occur at 2 hour intervals during the day and in small quantities. Gradually may be added broiled and roasted meats, including beef, lamb, poultry and nonoily fish. Potatoes (boiled, mashed, riced, or baked and without the jackets) may also be added. Fruits and other vegetables should be withheld pending the progress of the illness and should be added only if the clinical course justifies it. In the latter situation, some vegetables in puréed form may be tried. Last to be added are the cooked or preserved fruits. Raw fruit almost without exception should be omitted. Very ripe or baked bananas are sometimes beneficial in patients with steatorrhea. To be avoided also are the fried foods, veal, all pork products (except oven-broiled bacon), cabbage, cucumbers, onions, stews, gravies, pies, pastries, bran, candy, nuts, rhubarb, buttermilk, baked beans, ice cold food or drink, carbonated beverages, and oil dressings. Milk should be omitted unless it has been powdered or previously boiled.

This review of some of the problems to be considered in the diarrheas stresses the somatic component. It will be recalled that a large number of these individuals have functional diarrhea, and therefore the neurogenic or psychic factor is prominent. In this connection the management of the somatic features of the functional and organic diarrheas is similar, varying only as to the specificity of etiology. Intensive consideration is given the psychic and environmental features of the functional diarrheas. Thus proper regard should be given to domestic, financial, occupational and, particularly in the cases of infants and children, parental influences. In the latter instance an educational program is often productive of excellent results. A simple explanation to the parents of the natural physiology of spontaneous dejections and the unphysiologic approach by the use of laxatives may result in saving a child from a life of dependence on laxatives and resultant irregular and poor bowel function. But in patients who have organic diarrhea, regardless of the cause, the neurogenic element plays a significant role also. Therefore, in addition to the approach in correcting the somatic factors, appropriate and subtly conducted reviews of the environmental and psychic situations involved are indicated.

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Pediatrics IN GENERAL PRACTICE

For general practitioners, who handle more than 85 per cent of all pediatric care, POSTGRADUATE MEDICINE *here presents authoritative, up-to-date summaries by specialists in pediatric problems.*

Glycogen Disease

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IN the history of glycogen disease, 4 dates are of special importance: 1928, 1929, 1932 and 1952.

In 1928[1,2] we presented the first clinical and biochemical description of the condition known at present as the hepatomegalic type of glycogen disease. In that year we reported the observations in the case of a boy who was then 8 years old and whose metabolism showed peculiar disturbances. He was slightly stunted in growth but was much too heavy and gave the impression of a patient with adiposogenital dystrophy (Figure 1a). The liver was greatly enlarged; the spleen could not be felt. Acetone was often present in the day specimen of urine. In a fasting state the urine nearly always contained considerable acetone; also, a considerable quantity of beta-oxybutyric acid frequently was found. Moreover, in the fasting condition marked hypoglycemia was always present, without other abnormal clinical symptoms. After ingestion of 30 to 50 gr. of glucose, fructose or galactose, no sugar was excreted in the urine, even when the test was repeated within a few hours. Ketonuria, present in the fasting state, often disappeared slowly during these tests. After an injection of ADRENALIN®, there was only slight elevation of the blood sugar, but a marked increase in ketosis was noted as well as a decrease of the respiratory quotient. Further, the boy proved to be hypersensitive to very small quantities of insulin.

From these and other findings we concluded in 1928 that this was a condition hitherto unknown, which showed an accumulation of carbohydrates in the enlarged liver and perhaps also in the muscles in the form of glycogen, which could be mobilized only with great difficulty. Consequently the patient was constantly in a metabolic condition in which carbohydrates were difficult to mobilize. In this way the hypoglycemia and acetonuria could be explained, as well as the boy's preference for bread.

In 1929, more than a year after these conclusions were published, anatomic proof of our explanation of this condition was supplied by von Gierke[3] and the chemical proof by Schönheimer[3a] in the necropsy findings of

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2 children who during life also had had marked enlargement of the liver, but in whom hardly any of our metabolic examinations had been performed. In these children, enlargement of the liver and of the kidneys was found (hepato-nephromegalia glycogenica), due to an accumulation of glycogen which could be mobilized only with great difficulty.

In 1932 Pompe[4] was the first to describe a case in which there was enormous hypertrophy of the heart due to glycogen accumulation. He called the condition cardiomegalia glycogenica.

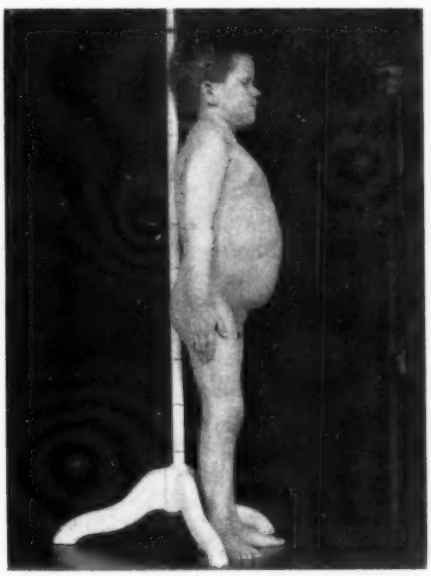
In 1952 G. T. Cori and C. F. Cori and their co-workers[5,6] found that the glycogen isolated from the livers of 10 patients with the hepatomegalic type of glycogen disease showed no abnormality of structure in 8 cases. In the remaining 2 the livers yielded glycogen that showed, in general, structures with much less branching of the glucose units than that from normal livers. By considering the enzymes in the liver necessary for the conversion of glycogen to glucose, the Coris found either an absence or a marked decrease of the enzyme glucose-6-phosphatase. While it is possible to explain the increase in glycogen in the livers of these patients by the absence of this enzyme,[7] the same reasoning cannot be applied to the abnormal accumulation of glycogen in skeletal or heart muscle, since glucose-6-phosphatase is normally absent from these tissues. A deficiency of some other enzyme may account for this.

Diagnosis

It was several years after the 1928 and 1929 reports before similar clinical and pathologic descriptions penetrated into the literature of other countries. Since then a large number of cases of the disease, mostly of hepatomegalia glycogenica and some of cardiomegalia glycogenica, have been described. In addition there are a number of reports of cases in which there is enlargement of more than one organ, due to accumulation of glycogen. Metabolic disturbances are found only in the hepatic form of the disease.

In 1932 we observed a second case of the hepatomegalic type of glycogen disease. This girl, then 5 years old, presented clinical and metabolic features which corresponded with those found in the boy (Figure 2a).

In 1933, after earlier researches of the Coris, we found that in both our patients the absence of an initial blood sugar elevation



FIGURES 1a and b. Photographs showing decrease in size of the liver in our first patient. a *(left)* 1928; b *(right)* 1948.

after the injection of adrenalin was particular evidence of the immobilization of glycogen in the liver. Absence of a normal elevation of the lactic acid content of the blood after the injection of adrenalin indicated an insufficient mechanism for mobilizing muscle glycogen. Other metabolic disorders found at that time in both cases were raised blood glycogen and hypercholesteremia.

As dissociation of disturbances in liver function is a well known phenomenon, we could expect that the series of cases of glycogen liver disease described in the literature would show a varying intensity of some of the symptoms. The pathologic picture is not always the same, with variation especially in the quantity of fat or connective tissue. For example, much fat was present in the first case described by von Gierke (1929) and in the cases of Krakower (1936). (Here it is useful to recall the name "hépatomégalies polycoriques" proposed by Debré[8] as a general term for enlargement of the liver caused by an accumulation of glycogen and/or fat.)

The parents of our first patient were consanguineous, a feature which has been observed by others in cases of glycogen disease. Moreover, frequently more than one case of glycogen liver disease or glycogen heart disease has been observed in the same family (Abramson and Kurtz[9]).

In the diagnosis of the hepatomegalic type of glycogen disease, chemical, histologic and histochemical study of a muscle biopsy may be as useful as liver biopsy, and a muscle biopsy is, of course, less dangerous.

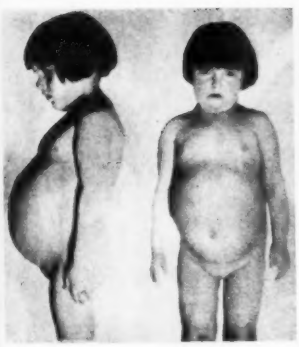
Differential Diagnosis

In discussing differential diagnosis of the hepatomegalic type of glycogen disease the case of Parnas and Wagner, described in 1922, is often mentioned. This also concerned a patient with marked hypoglycemia on fasting, always accompanied by acetonuria but without any symptoms. The liver was enormously enlarged. The authors had observed that after ingestion of various sugars there was hyperglycemia and glycosuria with disappearance of ketonuria, and they assumed therefore that the liver was not able to convert sugar into glycogen. Later the case developed into diabetes mellitus.

Cirrhosis of the liver, fatty liver, and the syndrome of Mauriac (1930) also had to be considered in our cases. Arguments against the diagnosis of cirrhosis of the liver were the absence of an enlarged spleen in both cases and the fact that various liver function tests showed no abnormalities. In our second case the urine often gave a positive urobilin reaction which could indicate that the liver, in addition to glycogen accumulation, showed slight cirrhotic changes.

Kramer, Grayzel and Salomon (1935) were the first to indicate the possibility that a greatly enlarged liver combined with certain metabolic disorders might also be caused by marked fatty infiltration of the liver. One of their cases showed a greatly enlarged liver, marked hypoglycemia and no increase of blood sugar after adrenalin injection. However, hypercholesteremia and ketonuria were absent, and this absence together with that of glycosuria after ingestion of a large quantity of carbohydrates indicated that the patient was able to utilize sugar.

Mauriac's syndrome or huge liver enlarge-



FIGURES 2a and b. Photographs showing decrease in size of the liver in our second patient. a *(above)* 1932; b *(right)* 1951.

ment in juvenile diabetes with delay in growth is seen in diabetic children, usually in those whose disease began at an early age. The syndrome may develop when the diet is maladjusted and uncontrolled and the quantity of insulin insufficient. Cases of Mauriac's syndrome differ from those of hepatomegalic glycogen disease in that in the former, hyperglycemia and glycosuria are present, whereas in the latter, hypoglycemia and usually a low curve in the glucose tests are seen. In addition, the epinephrine test gives different results in the two conditions. Mauriac's syndrome usually disappears in a few months with adjustment of diet and insulin.

Both our patients had symptoms which differed from those observed in other patients with chronic liver disease. Our concept was supported by the description after 1929 of some cases of glycogen liver disease in which the diagnosis had been confirmed by necropsy or biopsy and a clinical and biochemical picture found that was practically identical with that of our cases.

Since then, some cases of cirrhosis of the liver in children have been described in which some of the symptoms of glycogen liver disease were present. However, the presence of an enlarged spleen militated against the diagnosis of glycogen liver disease and, moreover, in some cases the liver proved to contain hardly any glycogen.

Some years ago Wagner[10] described the finding of an increased glycogen content of the leukocytes in the hepatomegalic type of glycogen disease, a factor which also should help greatly in diagnosis.

Cardiomegalic Type of Glycogen Disease (Pompe)

The cardiomegalic type of glycogen disease is much more difficult to recognize than the hepatomegalic type. As already mentioned, in the latter the disturbance of hepatic glycogenolysis especially is responsible for an important part of the biochemical findings. These findings are absent in cases of cardiomegalia glycogenica. In both forms, however, the accumulation of glycogen is not restricted to the organ which shows visible enlargement. In the cardiomegalic type the simultaneous accumulation of glycogen in the striated muscles is stressed, and sometimes they are equally enlarged. At present no other diagnostic test is available by which cardiomegalia glycogenica can be diagnosed during life, and in doubtful cases we have to rely on the appearance at biopsy of the vacuolar structure of the skeletal muscle fibers (Figure 3a and b) and on the histochemical demonstration of an abnormal quantity of glycogen in the muscle fibers.

Occasionally, more than one case of the cardiomegalic type of glycogen disease is observed in the same family, although less frequently than in the hepatomegalic form. The patients nearly always are young infants who do not thrive, and who have attacks of dyspnea and sometimes of cyanosis during feeding. In some cases the dyspnea and cyanosis occur suddenly, shortly before death. Physical examination usually discloses the heart to be grossly enlarged and the heart sounds to be normal. Anteroposterior roentgenograms show the heart to be greatly enlarged in all directions, with signs of pulmonary collapse or emphysema. Sometimes there is a soft systolic murmur at the apex. In various cases, impaired percussion with increased bronchophony and rhonchi has been noted, especially over the left part of the thorax. The liver shows little or no enlargement, although the

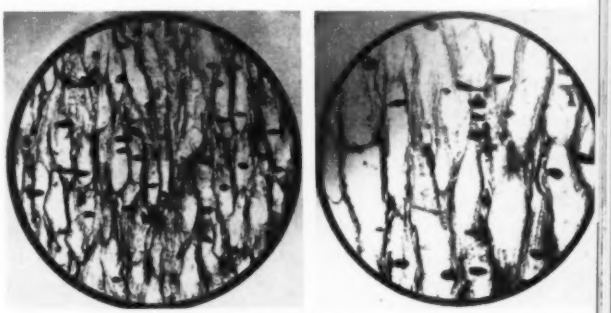


FIGURE 3a *(left)*. Aspect of the vacuolated heart-muscle fibers (Pompe). b *(right)*. Elongated vacuoles constituted by glycogen (Pompe).

spleen is sometimes palpable. Electrocardiograms are of little use in the differential diagnosis of cardiomegalia glycogenica.[11]

Conditions which must be differentiated from cardiomegalia glycogenica[11-15] are rhabdomyoma of the heart, cardiomegalia glycogenica circumscripta, anomalous origin of the coronary artery with areas of fibrosis and round-cell infiltration of the myocardium, and a group of obscure cases of cardiac enlargement belonging to so-called "idiopathic" cardiac hypertrophy in infancy. To the latter group belong subendocardial fibroelastosis, acute interstitial myocarditis (Fiedler's myocarditis) and essential hypertension.

Follow-Up of Cases

The patients in the 2 cases described by us in 1928 and 1933, respectively, are now 31 and 25 years of age. Neither their physical nor their mental development is retarded. The urine and the blood pressure are normal. In the case of the girl, who is now married, menstruation and secondary sexual development appeared at the normal time. The boy has been married for some years and is the father of a normal son. In both cases the liver has decreased in size (Figure 1b and Figure 2b) since puberty and is at present only just palpable. The boy's teeth were deciduous until he was 18 years old, when gradually they were replaced by permanent ones.

The special sensitivity to infections observed in other patients with glycogen disease has not been noted in our cases.

In the course of years the biochemical symptoms of these patients have been studied at intervals. In 1951 the fasting blood sugar content of the boy was practically normal but did not change after adrenalin injection. The urine in the fasting condition did not contain acetone, but 2 hours after injection of adrenalin the acetone reaction was slightly positive. The lactic acid content of the blood showed a slight temporary rise and the serum cholesterol was only slightly elevated.

Three years ago the young man underwent an appendectomy, at which time the muscle fibers in the wall of the removed appendix proved to contain large quantities of glycogen (Figure 4) (stained according to Best by Dr. R. van Dam).

In July 1951 the urine of the girl contained a trace of urobilin and, after adrenalin injection, only once a trace of acetone. The fasting blood sugar content was normal and did not rise during the first half hour after adrenalin injection, and after that it rose only slightly. The glycogen content of the blood was still increased and that of the leukocytes was at the upper limit of normal.

Both patients, therefore, still have some metabolic disorders similar to those found early in the course of their disease.

From these long-continued observations[20] it appears that the prognosis in glycogen disease of the liver is not necessarily unfavorable. In no case have we seen the transition into diabetes mellitus.

Etiology

Sufficient arguments exist in favor of the conception that at least in the hepatomegalic type of glycogen disease, hormonal factors are of great importance, next to a definite en-

FIGURE 4. Section of wall of appendix showing glycogen in muscle fibers.

zymatic lesion, as mentioned earlier in this discussion. Recent researches have stressed the possible significance of ACTH in glycogen disease.

Treatment

The combination of hypoglycemia and acetonuria in the hepatomegalic type of glycogen disease prompted us to prescribe a diet rich in carbohydrates and poor in fat. The oral ingestion of choline may have some influence on the ketosis, especially when there is reason to believe that the liver contains a great deal of fat as well as glycogen. Bridge and Holt[16] have recommended that these patients take an extra quantity of proteins in the evening. Lowrey and Wilson[17] found that in one case the symptoms of hypoglycemia were favorably influenced by administration of large quantities of proteins and small amounts of carbohydrates. Matheson[18] and other investigators observed the quick disappearance of ketonuria and reduction of the size of the abdomen after bile salts were given.

None of these therapeutic measures has any fundamental effect on the disease. Extensive experiences with ACTH and cortisone still are lacking. In a few cases in which ACTH was used, hypoglycemia and acetonuria disappeared during the period of therapy.[19]

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The Diagnosis of Acute Poliomyelitis

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The diagnosis of acute poliomyelitis can be the simplest or the most complex of problems. A typical clinical history preceding the onset of segmentally distributed paralytic manifestations at the time of epidemic incidence of poliomyelitis leaves little doubt in the mind of the physician. On the other hand, proper interpretation of findings and localization of neural damage can be most difficult although of great importance. For example, if ninth and tenth cranial nerve palsies are present, possible involvement of the nearby central respiratory center must be carefully watched for. Similarly, the correct interpretation of drowsiness or irrationality in a patient with respiratory difficulty may be crucial.

In actuality, the diagnosis is a clinical presumption based on certain physical signs, historic facts and suggestive laboratory findings, and follows exclusion of a number of commonly confusing conditions. There is, however, no physical finding, historic fact, or

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laboratory procedure which is in itself pathognomonic. Bacterial diseases can be categorized by identification of offending organisms from cultures which are available in most clinical laboratories. The diagnosis of viral diseases such as poliomyelitis, however, remains a task for the trained investigator and entails animal inoculation, tissue culture technics, or serologic methods which can be performed in relatively few laboratories.

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Paradoxically, research in the field of viral infections of the central nervous system has increased rather than reduced diagnostic difficulties. It has indicated that little can be accomplished in aborting or modifying the course or pattern of poliomyelitis after paralysis has occurred. It has revealed the presence of very frequent asymptomatic infections. Bodian[1] and others have taught us that viral proliferation in the central nervous system has reached a zenith on the first day of illness, but unfortunately this is not detectable by practical clinical means. The diagnostic tools which are available primarily support retrospective diagnosis and have been developed with relation to studies of immunity. Casals and Olitsky,[2] for example, have described a specific complement fixation test for poliomyelitis, culminating years of effort by several workers. But even this contribution is not in completed or final state, and certainly is not available generally as an aid to clinical diagnosis. Finally, the early presence of viremia in chronologic relation to the primary stage or first hump of the commonly biphasic clinical course has been clearly established and presents challenging possibilities in preventive management, but it has not simplified the problem of diagnosis.

In spite of the fruits of research, no substitute has yet been found to supplant the traditional technics of a competent clinician in reaching a diagnosis. By the same token, however, the physician has learned that his most discerning judgments are subject to great limitations. He knows that for every recognizable case, many individuals will have inapparent or subclinical infection with which he must be concerned but which he cannot definitely identify. Furthermore, since an appreciable percentage of paralytic cases can be prevented from developing more serious involvement by prompt supportive care, doctors are constantly faced with the problem of critically appraising a wide variety of apparently minor illnesses. The studies of Francis[3] would seem to indicate that inapparent forms of the disease are not universally distributed in a population, but rather that they tend to occur primarily among family and other intimate contacts. From this work it follows that pertinent and carefully elicited historic data may be especially helpful in supporting a questionable diagnosis.

The symptomatology of abortive forms of poliomyelitis differs in no important respect from that of any brief febrile "flu-like" illness. The occurrence of sore throat, headache, malaise, loss of appetite and often some nausea or vomiting during the summer months is most suggestive, particularly when there is a high incidence of recognizable poliomyelitis in the community. Temperature elevations to 101 to 102° F. can be expected, and abdominal pain as well as constipation are frequently present. Conspicuous by their absence are cough, coryza, pharyngeal exudate or membrane, diarrhea or localized abdominal tenderness and rigidity.

If, in addition to a suggestive combination of general findings, stiffness of the neck and back appears and muscle pain of variable severity and distribution is recognized, the term nonparalytic poliomyelitis is applicable. Lumbar puncture in most patients reveals an increase in cells as well as in protein. The necessity of performing this procedure routinely is open to question, but certainly the information obtained justifies it when any real doubt exists. It must be remembered, however, that even in paralytic forms of the disease, abnormalities of the cerebrospinal fluid may not appear for 2 or 3 days. Values

for spinal fluid protein vary from 45 mg. per cent to 600 mg. per cent, and peak values are usually reached in approximately 6 weeks.[4] Protein levels tend to be higher in paralytic than in nonparalytic cases. The total cell count may vary within wide limits and rarely exceeds 1000 per cubic millimeter. More frequently there are less than 200 per cubic millimeter, and pleocytosis begins to subside after the fourth day in paralytic cases.[5]

To complete the picture of classic poliomyelitis, muscular weakness and/or paralysis is then superimposed on the symptomatology of nonparalytic forms. Paralytic manifestations are of infinite variety, no two cases being entirely similar in distribution or extent of involvement. Rarely, paralysis is so widespread as to obscure its characteristic distribution with relation to segments of the spinal cord, or diagnosis will rest entirely on identification of dysfunction in cranial nerve nuclei. Deep tendon reflexes in affected parts are depressed or absent, paralysis is flaccid and sensory disturbances are conspicuous by their absence. Finally, constipation and difficulty in micturition occur with considerable frequency early in poliomyelitis. Diarrhea, on the other hand, rarely occurs and in fact suggests consideration of other diagnoses.

A detailed and chronologic description of any illness is always of greatest diagnostic import. In as many as one-half the cases a biphasic course can be recognized. This is particularly true among children. First a vague illness of 2 to 3 days' duration occurs with temperature elevation to 100 to 101° F. and often with headache and general malaise. Diffuse pharyngeal hyperemia without signs of respiratory infection is frequently noted. After 1 to 3 days apparent recovery occurs; then after a latent period of several hours to 5 days similar symptoms recur and the "major illness" begins. This second temperature elevation is usually in the range of 101 to 103° F. Headache which had been relatively mild in the preceding "minor illness" now becomes quite severe, and nuchal rigidity develops. Resistance to straight leg raising and head drop when the shoulders are raised from the bed when the patient is supine also may appear. Because of stiffness of the back as well as of the neck, a patient stretches his extended arms behind him for support in attempting to assume a sitting position and even so is unable to bring himself fully erect. The resulting propped position is described as the "tripod sign" and is sufficiently characteristic to be of diagnostic help.

Muscular fasciculations or tenderness may precede the onset of paralysis at any time after the beginning of the "major illness," and, in general, the progression of paralytic involvement parallels the febrile course. As a corollary, paralysis seldoms appears after the temperature has returned to normal.

Thus far diagnosis has been considered largely from the standpoint of identifying an illness as poliomyelitis. Of even greater importance to the individual patient is early recognition of neural lesions which affect respiration. These may be paralysis of the muscles of respiration, involvement of the respiratory center in the midbrain, or lesions of the lower cranial nerves. Ninth and tenth nuclear lesions, as prime examples, may result in dysphagia and obstruction of the airway by pooling of secretions in the hypopharynx and by loss of the gag reflex. If, in addition, respiratory muscle paralysis results in a loss of the ability to cough, a double threat exists. In any event, compromise of the airway must be anticipated by proper diagnostic interpretation of such minimal findings as a nasal twang to the voice or difficulty in swallowing a small piece of toast. Too often consideration of airway obstruction is delayed until fluids are regurgitated through the nose and until respiration is involuntarily shallow in defense against the imminent threat of aspirating pooled secretions.

Two general methods of maintaining pulmonary ventilation are available to us, namely, clearing the airway of obstruction and artificial respiration. Either measure alone may be sufficient in an individual case, but it is important to re-emphasize that artificial respiration cannot be effective unless the airway is patent. More can be accomplished if an early diagnosis of ventilatory insufficiency is suspected from typical restlessness, an in-

crease or considerable variability in pulse rate and blood pressure, the appearance of flushing, or mildly disturbed consciousness than if cyanosis, coma, convulsions or apnea dictates heroic measures.

The measurement of tidal volumes or vital capacity as a diagnostic technic facilitates detection of respiratory impairment before dangerous reduction in function has occurred. Even the simple expedient of requesting the patient to count as far as possible without taking a breath or listening with a stethoscope at the nose and mouth may give early information as to reduced respiratory function and perhaps as to patency of the airway. Inspection for thoracic excursion with respiration, palpation of the costal margins for expected downward movement of the diaphragm during inspiration, and careful note of retraction, whether suprasternal, infrasternal or intercostal, are also important.

Paralysis of abdominal musculature, particularly in young children, adds greatly to respiratory distress and may be recognizable as greatly increased prominence of the abdomen during inspiration. Also the careful observer is alert for paralyses which indicate neural damage in spinal segments which innervate important respiratory musculature. For example, deltoid paralysis is often the harbinger of respiratory muscle paralysis. Similarly, in dealing with bulbar poliomyelitis, involvement of the ninth and tenth cranial nerves puts one on guard for evidence that nearby respiratory centers of the brain stem may have become affected.

There is an understandable tendency to think of respiration primarily as a means of effecting oxygenation and therefore to feel secure if ample oxygen is given. However, the adequacy of pulmonary ventilation is also of crucial importance. Prolonged hypoventilation with excessive accumulation of carbon dioxide may result in assumption of respiratory control by the carotid body. In other words, the central respiratory center becomes refractory to abnormally high concentrations of carbon dioxide and respiration must then be regulated by the cruder stimulus of hypoxia. Under such circumstances, as described by Sarnoff and Whittenberger,[6] the physician must recognize the need for increased ventilation as well as for increased oxygenation. If oxygen alone is given the blood oxygen content can be raised sufficiently so that reflex respiratory stimulation from hypoxia no longer occurs. Since carbon dioxide is not being removed from the lungs by normal tidal exchanges, the levels of it in the blood remain abnormally high and, in fact, may exceed concentrations to which the central mechanism for control of respiration can react. If, however, good respiratory excursions are provided while oxygen is being given, blood levels of carbon dioxide will be reduced rather rapidly to normal levels as oxygenation is increased.

Summary and Conclusion

The diagnosis of poliomyelitis, though relatively simple in classic epidemic form, can be most difficult to support in sporadic, atypical or less obvious situations. Research in poliomyelitis has not yet afforded a single reliable diagnostic tool which is practical for general clinical use. Nonparalytic and abortive forms must be suspected largely on the basis of symptomatology; once suspected, support comes from careful evaluation of epidemiologic data, physical findings, and usually by careful examination of the cerebrospinal fluid.

In the presence of paralyses which may lead to respiratory impairment, particularly discerning diagnostic judgment is necessary. First, obstruction of the airway must be recognized and corrected as early as possible. Second, in evaluating respiratory function, whether artificially supported or not, due consideration from a diagnostic point of view must be given not only to oxygenation but also to carbon dioxide excretion.

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Tumors of the Stomach

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ANY presentation of tumors of the stomach is of considerable interest because a large majority of gastric tumors are carcinomas.

The early recognition of gastric tumors is of special importance because the curability rate after treatment of gastric carcinoma is so small and the five year survival rate is directly related to earlier diagnosis and, probably of equal importance, to a more radical surgical attack such as total gastrectomy.

Adapted from an exhibit shown at the annual meeting of the American Medical Association.

CLASSIFICATION

BENIGN TUMORS

A. Leiomyoma

B. Mucosal polyps
Adenoma (solitary, multiple)—of particular interest because so many are malignant or ultimately become malignant. In our experience, 30 per cent were malignant at the time of excision. Consequently, many of them have to be treated as either actual or potential carcinoma of the stomach.

C. Miscellaneous
1. Lipoma
2. Fibroma
3. Neurofibroma
4. Hemangioma
5. Aberrant pancreas

D. Inflammatory
Giant hypertrophic gastritis
Pseudopolyposis

MALIGNANT TUMORS

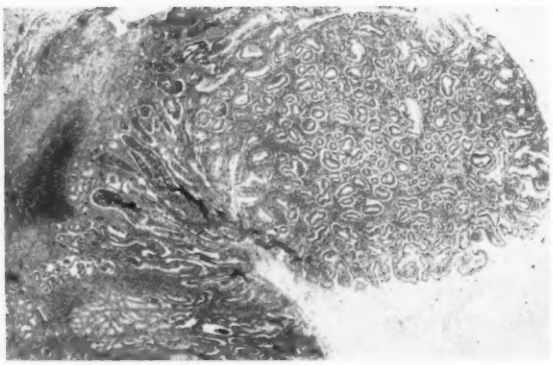
A. Carcinoma
1. Adenocarcinoma
2. Carcinoma simplex
3. Linitis plastica
4. Mucinous

B. Sarcoma
1. Smooth muscle
Leiomyosarcoma
2. Lymphoid tumors
a. Lymphosarcoma
b. Reticulum cell sarcoma
c. Malignant lymphoma
d. Hodgkin's disease
3. Miscellaneous (rare)
a. Nerve tissue
b. Fibrous tissue
c. Vascular tissue

FIGURE 1. Solitary polyp arising from lesser curvature. a. Microscopic cross section. b. Spot film showing polyp.

Benign Tumors

1a



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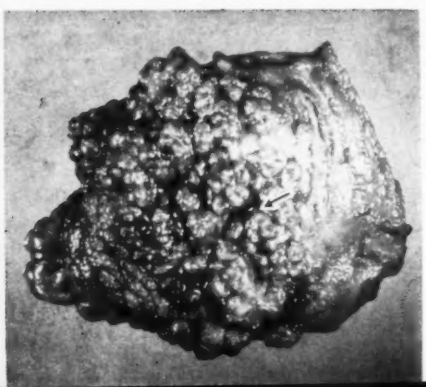


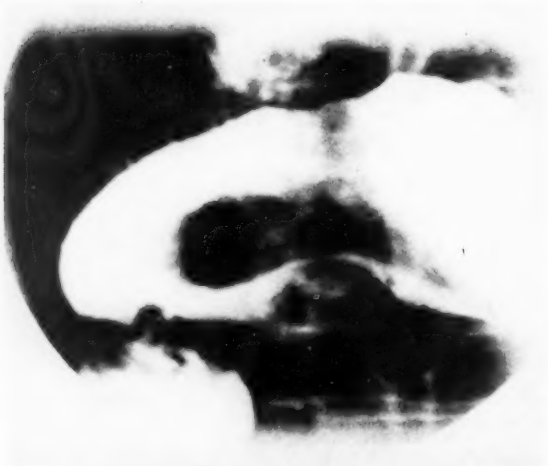


FIGURE 2 *(left, above)*. Extensive multiple polyposis. *Below*. Open specimen; arrow indicates area of malignant degeneration.

Adenomatous Polyps

The outstanding symptoms of polyps, particularly in the prepyloric area, are obstruction due to prolapse into the duodenum, achlorhydria and anemia. In the group of miscellaneous tumors, aberrant pancreas is of particular interest because such tissue is occasionally seen in the pyloric end of the stomach or in the first part of the duodenum. Operation is necessary because the filling defect as evidenced by roentgenologic examination is easily confused with a benign polyp or malignant tumor. Most of these tumors are subserosal and present a submucosal dimple with a rudimentary duct entering the aberrant pancreatic tissue. Many of them can be excised locally, and resection is not necessary if their true nature is recognized from the gross appearance.

Symptoms

1. Hemorrhage
2. Motor disturbance
3. Pain
4. Obstruction
5. Achlorhydria

Treatment

1. Local excision
   a. Frozen section
2. Radical resection (where indicated)
   a. Partial
   b. Total

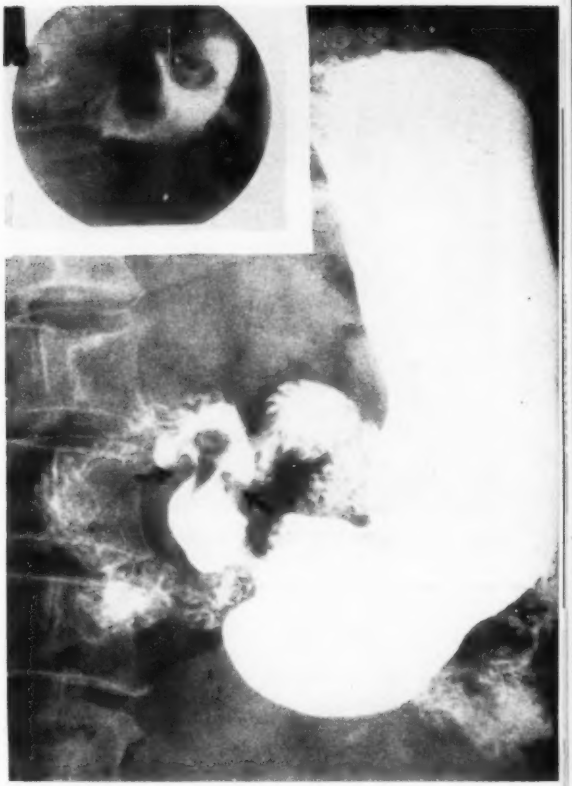


FIGURE 3. Polyp arising in prepyloric area, prolapsing into duodenum.

FIGURE 4 *(right)*. Polyp arising in pylorus, extending into duodenum.

FIGURE 5. Large lipoma in prepyloric area.

FIGURE 6. Aberrant pancreas in prepyloric area with dimple at opening of duc

Ulcer versus Carcinoma

FIGURE 9. Small malignant ulcer, lesser curvature.

FIGURE 10 *(right)*. Benign prepyloric ulcer perforating into liver. Preoperative diagnosis: carcinoma.

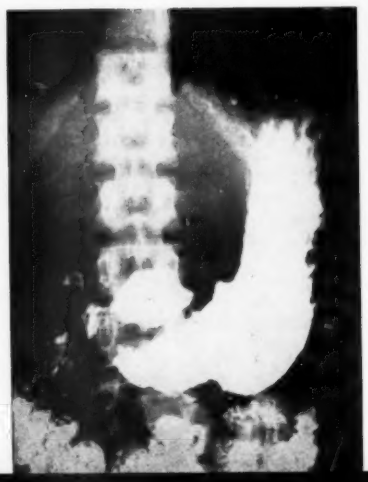


FIGURE 11 *(right)*. Benign ulcer on greater curvature. *Insert*. Lateral view showing penetration.

FIGURE 7. Leiomyoma of pars media.

FIGURE 8. Perineural fibroma; partial gastrectomy.

Since benign gastric ulcers, as well as benign gastric tumors, have been regarded as precursors of cancer, we must discuss peptic ulcer of the stomach in this light. It is doubtful whether more than a very small percentage (5 per cent) of gastric ulcers degenerate into carcinoma. In a series of 600 cases of gastric ulcer, 19.6 per cent of those in which operation was performed proved to be carcinoma on pathologic examination. The incidence of carcinoma in the entire group treated medically and surgically is about 10 per cent. The location of the ulcer—whether prepyloric, on the greater curvature or along the lesser curvature—does not enable the roentgenologist to make an accurate decision as to whether or not the tumor is malignant. We have had 11 instances of benign gastric ulcers on the greater curvature. Likewise, we have seen benign ulcers in the prepyloric area. These two areas, the greater curvature and the prepyloric area, are prone to carcinoma. The size of the ulcer also does not assist materially in deciding whether the ulcer is malignant or benign. The average age of patients with benign ulcer is approximately 54 years, whereas the average age of those with carcinoma is 57 years.

Incidence of Malignancy in Gastric Ulcer

	Per Cent
Operated cases	20
All cases	10
Pre-existing ulcers	5.7

Presumptive Evidence of Malignancy

1. Greater curvature
2. Associated achlorhydria
3. Failure to heal under medical treatment
4. Recurrence

Distinction Cannot Be Made Conclusively by

1. X-ray contrast studies
2. Gastroscopy
3. Size and location
4. Inspection or palpation at operation

Treatment

1. Hospital control, three weeks
2. Subtotal gastrectomy necessary for:
   a. Failure to heal
   b. Location on greater curvature or antrum
   c. Recurrence of ulcer
   d. Suspicion of malignancy

FIGURE 12. Benign ulcer on greater curvature; resection specimen of Figure 11.

FIGURE 13. Small superficial malignant ulcer on lesser curvature; total gastrectomy.

FIGURE 14. Benign ulcer of antrum with chronic gastritis; resected specimen.

FIGURE 15 *(left)*. Large benign ulcer on lesser curvature; healed under medical treatment.

FIGURE 16 *(right)*. Recurrent ulcer three years later; partial gastrectomy. Resection because of recurrence. Pathologic examination: benign.

Carcinoma

HISTORY

- Epigastric distress
- Anorexia
- Weight loss
- Fatigue
- Indigestion
- Constipation

PHYSICAL SIGNS (None Early)

- Anemia
- Epigastric mass
- Nodular liver
- Virchow's node
- Rectal shelf
- Ascites
- Cachexia

ROENTGENOLOGIC FINDINGS

- Rigidity
- Interference with peristalsis
- Crater
- Filling defect
- Obstruction

GASTRIC ANALYSIS

- Achlorhydria
- Red blood cells
- Tumor cells

Carcinoma is much more common in men than in women, and 90 per cent of our patients were more than 40 years of age. It is of great importance, therefore, to be suspicious of the possibility of gastric carcinoma, particularly in men past the age of 40. Any person who has epigastric distress, weight loss, anorexia or any type of indigestion should have very careful roentgenologic and gastroscopic examinations and other special tests to rule out gastric carcinoma, particularly if symptoms persist after correction of the diet and simple therapeutic measures fail to relieve the distress. The most prominent symptoms are simple indigestion, vague epigastric distress and anorexia. Marked weight loss, nausea and vomiting, anemia, evidence of blood loss, etc. are symptoms of advanced carcinoma, and most cases with these symptoms are inoperable on exploration.

DEATHS FROM CARCINOMA OF STOMACH

(Vital Statistics, United States, 1948)

Total number of deaths	26,215
Rate per 100,000 population	17.9 per cent
Men	11.15
Women	6.75

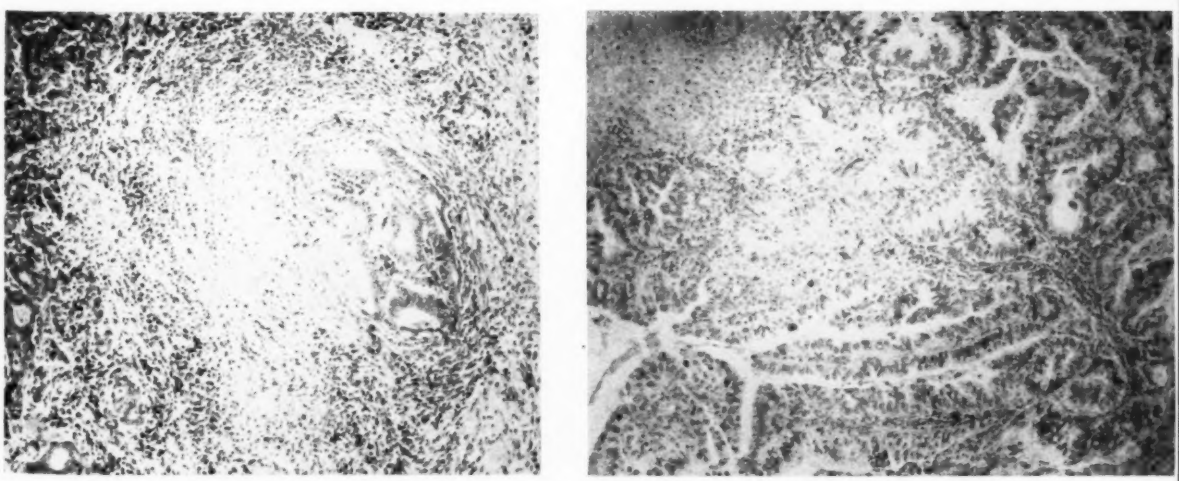


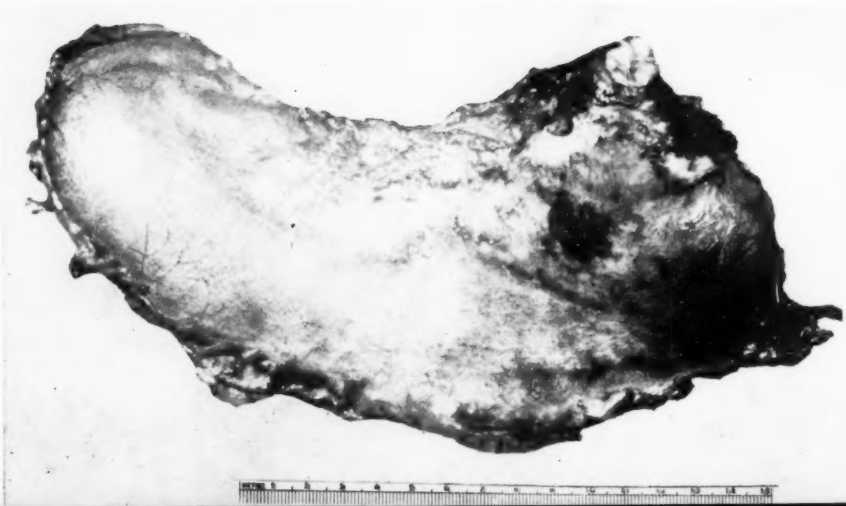
FIGURE 17. Photomicrographs. *(left)* Adenocarcinoma of stomach; *(right)* papillary adenocarcinoma of stomach.

FIGURE 18. Adenocarcinoma, antrum; partial gastrectomy; *(right)* open specimen.

FIGURE 19 *(left)*. Small malignant ulcer, lesser curvature. Symptoms of one month's duration; partial gastrectomy. Lymph node metastases present.

FIGURE 20 *(right)*. Carcinoma of cardia; total gastrectomy; patient lived seven and a half years after surgery.

FIGURE 21 *(right)*. Linitis plastica. Total gastrectomy; stomach rigid and contracted.



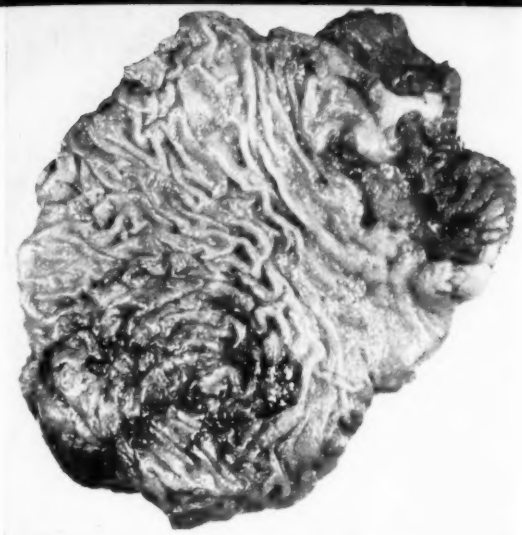


FIGURE 22. Carcinoma of antrum; partial resection.

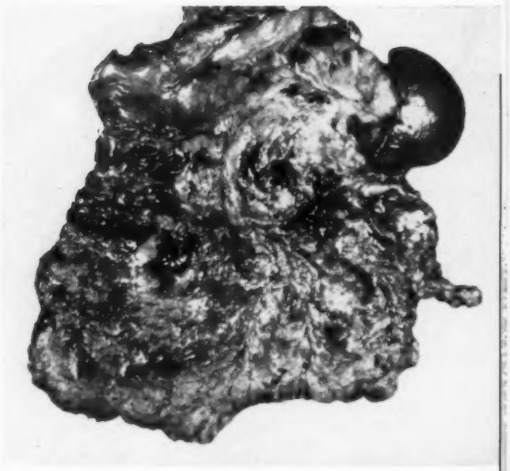


FIGURE 23. Total gastrectomy; resected specimen showing entire stomach, spleen and omentum.

FIGURE 24 *(left)*. Open specimen, total gastrectomy.

FIGURE 25 *(left below)*. Stenosis of esophagojejunostomy following total gastrectomy for carcinoma. Note dilatation of esophagus. FIGURE 26 *(right below)*. Note absence of distention of esophagus following dilatation of stoma.

Sarcoma

FIGURE 27. Large spheric filling defect in upper half of stomach.

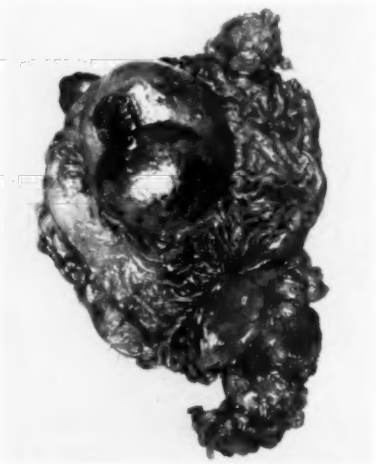


FIGURE 28. Large circumscribed tumor with superficial ulceration.

Sarcoma of the stomach can develop from any of the mesenchymal elements of the gastric wall, but in general it arises only from lymphoid and smooth muscle tissue. A tumor that develops from smooth muscle tissue is a leiomyosarcoma, whereas tumors arising from lymphoid tissue are divided into four groups according to Dr. Shields Warren's classification: (1) lymphosarcoma, (2) reticulum cell sarcoma, (3) malignant lymphoma and (4) Hodgkin's disease. Tumors that derive from other elements of the stomach wall, such as nerve tissue, fibrous tissue and vascular tissue, are extremely rare.

Leiomyosarcomas are relatively benign tumors and rarely metastasize, although we have seen 2 instances of metastases to the liver. In a series of 12 resections for leiomyosarcoma there was no recurrence.

The survival rate for patients with tumors arising from lymphoid tissue is much higher than that for patients with carcinoma. In our experience the survival rate after five years has been 54 per cent. Should a tumor prove to be inoperable, a biopsy should always be taken. Many large, bulky tumors are likely to be lymphosarcomas, and if they prove nonresectable at the time of laparotomy the patients in some instances can be treated effectively with deep x-ray. Leiomyosarcomas ulcerate early and the patients often have anemia or give a history of profound hemorrhage. Digestive symptoms rarely develop. These tumors are round, well delineated and intraluminal. Usually the diagnosis can be established from the roentgenogram.

Figures 27 and 28 show the roentgenographic appearance of a leiomyosarcoma in the resected specimen.

PATHOLOGY

	Number of Cases	
Leiomyosarcoma		9
Lymphoid tumors		32
Hodgkin's disease	10	
Reticulum cell sarcoma	6	
Lymphosarcoma	12	
Malignant lymphoma	4	
TOTAL		41

TYPES OF OPERATION

	Leiomyosarcoma	*Lymphoid Tumors*
Exploration and biopsy	0	4
Excision	2	0
Partial gastrectomy	5	19
Total gastrectomy	2	9
TOTALS	9	32

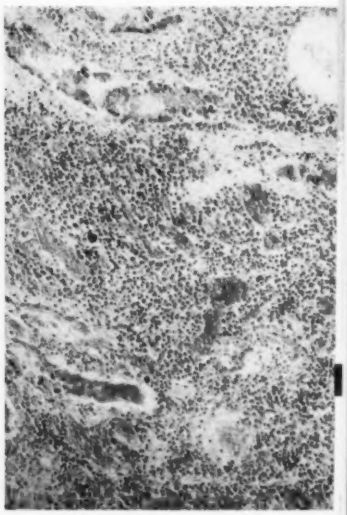
FIGURE 29. Recurrent leiomyosarcoma two years after local excision. Secondary resection.

FIGURE 30 *(left)*. Huge leiomyoma treated by local excision; patient well after 12 years.

FIGURE 31 *(right)*. Postoperative appearance of stomach 12 years after excision.

FIGURE 32. Lymphosarcoma of greater curvature; partial gastrectomy.

FIGURE 33 *(left)*. Gastric lymphosarcoma; patient alive 11 years after total gastrectomy; *(right)* photomicrograph of lymphosarcoma.



SURVIVAL

Leiomyosarcoma (No Operative Mortality)

Patients living and well*

2 to 5 years	3
6 to 10 years	2
11 to 20 years	4
	9

*One patient died six years after partial gastrectomy (cause unknown).

Lymphoid Tumors (20 Operative Deaths)

Patients living and well

6 months to 3 years	6 (20 per cent)
5 to 10 years*	11 (34.5 per cent)

Dead

6 months to 2½ years	14 (50 per cent)

*One patient with Hodgkin's disease is living and well seven and one-half years later with x-ray treatment alone.

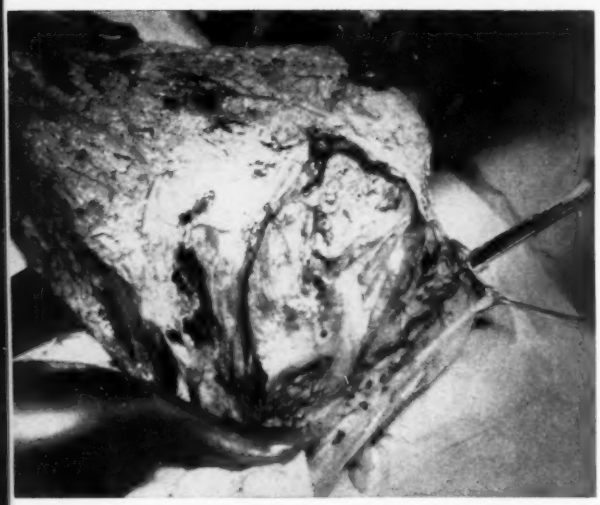


FIGURE 34. Omentum detached from transverse colon, opening lesser omental cavity. The stomach wall is visualized and the extent of the tumor can thus be determined.

FIGURE 35. Duodenum divided with cautery after mobilization of gastric curvature.

FIGURE 37. Clips have been inserted with Von Petz clamp and stomach is transected with cautery between two rows of clips; partial gastric resection.

Surgical Technic

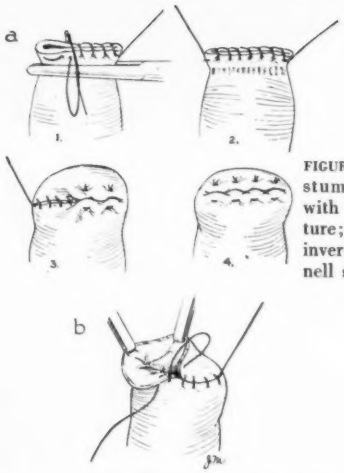


FIGURE 36. Duodenal stump closure: a. with clamp in suture; b. open end inverted with Connell stitch.

MORTALITY RATES

	NUMBER OF CASES	DEATHS	
		Number	*Per Cent*
Partial Gastrectomy			
1930-1935	60	24	40.0
1936-1940	116	19	16.3
1941-1945	179	17	9.6
1946-1951	175	8	4.6
Total Gastrectomy			
1927-1940	24	7	29.1
1927-1944	73	23	31.5
1944-1950	95	8	8.0
Transthoracic Gastrectomy			
	44	5	11.3

SURVIVAL RATES

	Per Cent
Partial gastrectomy	
Five years or more	26.7
Total gastrectomy*	
Less than two years	70.0
More than three years	23.3
Five years or more	12.5

*Total gastrectomy in this group done for advanced carcinoma.

In an effort to increase the survival rate after surgical removal of a malignant tumor of the stomach, total gastrectomy has been increasingly employed.

If the tumor is in the ampullary or the lower portion of the stomach, high radical partial gastrectomy can be done, but in all instances the omentum and the spleen are removed and care is taken to remove groups of lymphatic nodes whenever possible.

For tumors that involve the lesser curvature or extend high along the stomach, total gastrectomy must be done in order to insure removal well beyond the extent of the tumor. It must be remembered that malignant tumor in the stomach not only spreads to the lymph nodes but that there is also a general lymphatic spread through the wall of the stomach, a vascular spread and a spread into the duodenum. In radical removal of the stomach the duodenum is transected almost down to the ampulla of Vater. Likewise, in an increasing number of cases total gastrectomy must be employed in order to be certain that all tumor is removed because the extent of the tumor in the wall of the stomach cannot be determined from the gross appearance of the lesion at the operating table. With increasing use of total gastrectomy we hope that curability of cancer of the stomach will definitely be increased. It has been demonstrated that, at present, the mortality following total gastrectomy is comparable to that of partial gastrectomy. In the experience of the Lahey Clinic the mortality associated with partial gastrectomy has been 5.6 per cent, and in the last few years in a series of 190 cases the mortality of total gastrectomy has been reduced to 7 per cent.

In order to determine whether a tumor is resectable, the omentum is detached from the transverse colon, the stomach turned cephalad and the lesser omental cavity inspected. The extension of the tumor to surrounding organs can easily be determined by direct vision, and if the tumor proves to be inoperable the stomach with its omentum attached can be laid back to its normal position and the abdomen closed. Resection should be carried out provided the tumor is technically resectable, even though the organs involved by extension must be excised. In such cases a large portion of the pancreas can be removed, the spleen should always be taken out, and the left lobe of the liver and transverse colon also are resected when they are involved by direct extension of the gastric neoplasm.

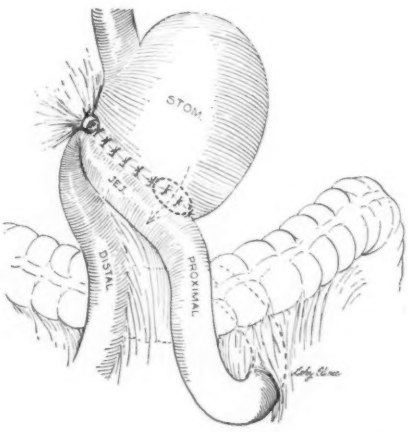


FIGURE 38. Partial gastric resection; note position of jejunal loop.

TOTAL GASTRECTOMY

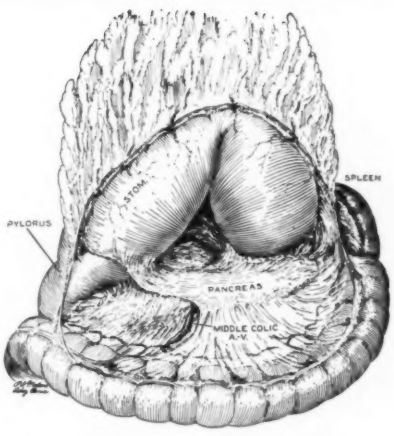


FIGURE 39. Omentum detached from colon; stomach turned up.

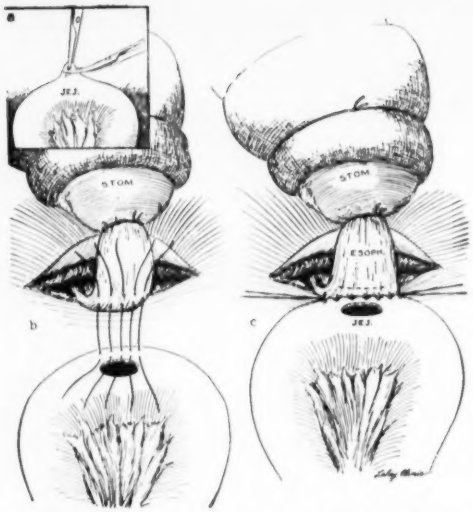


FIGURE 40. Total gastrectomy; esophagojejunal anastomosis.

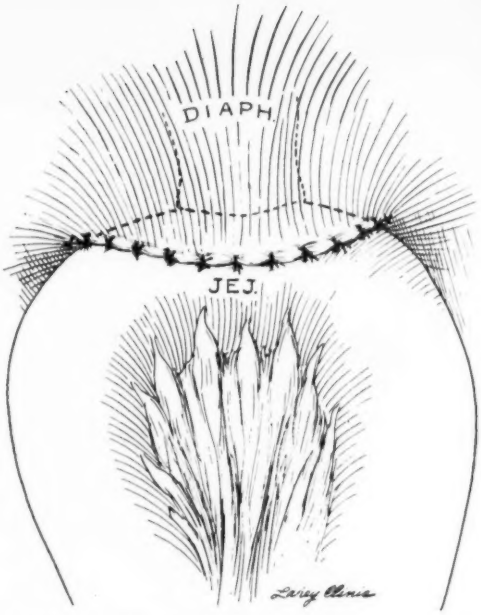


FIGURE 41. Esophagojejunostomy completed; anastomosis reinforced and suspended with peritoneal flaps from diaphragm.

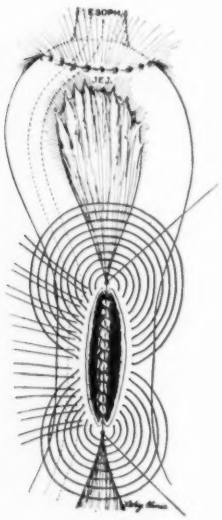
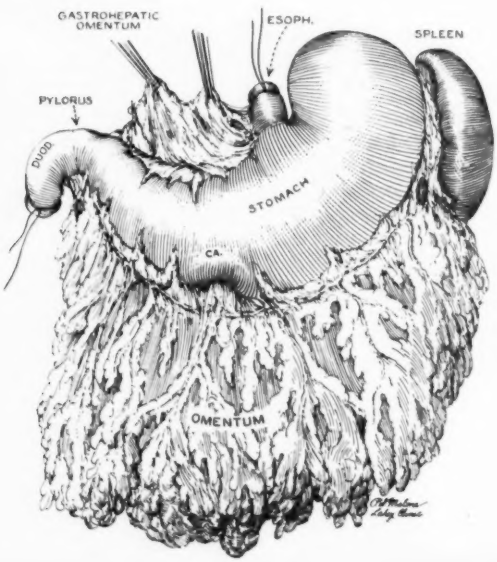


FIGURE 42 *(left)*. Enteroenterostomy for food pouch. Note anterior sutures placed and retracted before jejunal loops are open.

FIGURE 43 *(below)*. Total gastrectomy; specimen showing omentum, spleen, part of duodenum and esophagus removed with stomach. Carcinoma of the greater curvature.



SUMMARY

In the light of our present knowledge the only method of treatment of cancer of the stomach is surgical extirpation. Any hope of increasing the five year survival rate of patients with this type of malignant disease will depend on earlier diagnoses and more radical surgery. It is interesting to note that in the group of patients who have had total gastrectomies and whose course has been followed for five years or longer, 1 in 8, or 12.5 per cent, are alive after five years. It must be remembered, however, that these are advanced cases and that only total gastrectomy offered any hope of survival. It is possible that with utilization of the more radical procedures such as total gastrectomy in earlier cases, the survival rate may be notably improved. With the employment of partial gastrectomy approximately 1 patient in 4 is alive after five years. We believe that with the lowered mortality of total gastrectomy and the hope of a higher percentage of five year survivals with the use of more extensive operations such as total gastrectomy, a higher curability rate for cancer of the stomach may be obtained.

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PRIMARY CLOSURE IN PROCTOLOGY

ALL modern textbooks on proctology describe methods which depend on healing by second intention. Such methods are now obsolete in other parts of the body. The acceptance of healing by second intention in proctology is therefore a challenge to modern surgical technics. The bogey of sepsis from fecal contamination is the main objection to the use of primary closure, but insufficient emphasis has been laid on the resistance of healthy tissues and on the power of modern antibiosis.

The greater postoperative comfort, the absence of "laudable pus," the shortened convalescence, and the avoidance of prolonged packing and digital dilatation must surely commend themselves to progressive surgeons. The attainment of primary healing, however, requires a degree of surgical care and precision which some surgeons may not be prepared to devote to this problem.

The principles upon which primary closure is based may not be discarded without penalty and should be closely followed:

1. The bowel must be prepared as for colonic resection using oral and parenteral antibiosis combined with washouts.

2. Only fresh tissue may be sutured and this without tension (scar, fistulous tracks, and fibrosed fissures are detrimental to primary union).

3. Hematoma must be scrupulously avoided for its eradication is essential to healing.

The application of these principles is rendered easier if the jackknife position is employed during operation and if prolonged local anesthesia is used to induce postoperative comfort.

The ligation of the hemorrhoidal pedicle is achieved by "dissection" as opposed to mass ligation, the component vessels being ligated with 000 chromicized catgut. The edges are sutured without tension using a running 000 catgut suture. The Whitehead procedure involving removal of the pile-bearing area is thus possible without subsequent stricture. In these cases the secondary hemorrhoids are dealt with simultaneously and the circumference of the wound is closed with three sutures, each closing one-third in deltoid fashion.

The defect after radical fissure excision may be satisfied by rotating a pedicled skin flap and fixing it in position with interrupted 000 chromicized catgut sutures.

The most difficult problem in primary closure of anal and perianal wounds is that of recurrent fistula in ano. After eradicating all scar and fistulous track, the resulting cavity is filled with a fat or fat-muscle flap from the buttock. A drain is inserted and used to instill proteolytic ferments. Thus hematoma formation is avoided. This is very important for the low viability of these tissues and the infection which thrives on a ready nidus viti-

ate a satisfactory outcome. No tension is permissible throughout these procedures.

Now that antibiosis and familiarity with methods of satisfying tissue defects have greatly increased the possibility of obtaining healing by primary intention, prejudice and tradition should not be permitted to persist for long with healing *per secundam.*

KENNETH W. STARR

ESTROGENS IN CANCER OF THE BREAST

In a preliminary report,* Dr. Thomas L-Y. Dao of the Ben May Laboratory for Cancer Research of the University of Chicago has pointed out that estrogens are known to be involved in the origin of cancer of the breast in mice. Evidence has been produced that ovariectomy sometimes causes a remission of cancer of the breast in women, and Huggins and his associates have established that bilateral adrenalectomy with maintenance on cortisone acetate produces a regression of mammary cancer in women whose ovaries have been removed, although not in every instance.

A number of recent investigations have been concerned with the amount of estrogen in the urine of women under a variety of conditions. Recent studies confirm previous investigations to the effect that the urinary excretion of estrogens in premenopausal women was in the same range regardless of the presence or absence of breast cancer. Elimination of the function of the ovaries by roentgen irradiation or by removal of the ovaries led to lowered values of estrogen excreted in the urine, sometimes reducing the amount by one-half. Then, when an adrenalectomy was performed after the elimination of the function of the ovaries, estrogen was no longer detectable in the urine.

In the present series, 9 of 12 women with cancer of the breast who had been subject to bilateral adrenalectomy showed an actual measurable decrease in the extent of the cancer after the operation. This regression was observed in the cancer of the breast itself, in metastases in bones and in involvement of the pleura. The investigators feel that patients with cancer of the breast whose ovarian function has been eradicated still excreted estrogen in significant amounts, but that bilateral removal of the adrenals eliminated the estrogen from the urine. Hence they conclude that the adrenals are the only significant source of estrogen in women with breast cancer who do not have active ovarian function. They do not believe it is possible to state from the study that the reduction of estrogen was the critical factor in the remission of the disease.

MORRIS FISHBEIN

*Dao, Thomas L-Y.: Estrogen excretion in women with mammary cancer before and after adrenalectomy. Science 118:21-22 (July 3) 1953.

THE LANGUAGE OF MEDICINE

In a recent study on the influence of language on medicine Professor J. Z. Young[1] of the Department of Anatomy in the University of London says man is a social animal and a great talker. Much of the writing of men both in and out of science is a reflection of the evolution of the use of words to express ideas; since the ideas were frequently unscientific, the words used become equally unscientific.

Medical semantics have also interested Dr. Ffrangcon Roberts[2] whose essay on "Lingua Medica" in the *British Medical Journal* gives many instances to prove the point just made. The language of medicine obviously reflects historically the ideas of disease held as long as 2500 years past. Men have had to find names for what they observed. The principal sources of medical words lie in the ancient history of medicine, the most prolific source being the Greek component which was derived from Egyptian and Asiatic sources. The Romans employed Greeks as their physicians and most of the physicians of ancient Rome used both Greek and Latin words according to convenience.

In his interesting essay Dr. Roberts gives excellent examples of words derived from all the sources that have been mentioned. He calls attention, incidentally, to the manner in which even these basic words changed

with the migration of people. For instance, the word "shingle" comes from the word "cingulum" which was a belt and which, of course, reflected the manner in which shingles surround the body. Interesting is the word "acromegaly" which means literally "large ends" and refers to the large hands and feet of the acromegalic giant. Quite different from the stream of classic culture was the development of German words which did not have the relationship to classic origin so that the German has to define an ulcer as the "zwölffingerdarmgeschwür" which means the-12-finger-intestine-ulcer and "wormfortsatzentzündung" for appendicitis, the German word meaning wormlike-projection-burning.

All the ancient Greek words which describe the humoristic conception of medicine became indelibly imprinted in the speech of medicine so that sanguine, phlegmatic, choleric and melancholic persist and also hysteria, hypochondria, spleen and eczema.

Dr. Roberts' article is full of interesting examples of the manner in which medicine picks up its words from the general language and the verbal inaccuracies which result. Thus we have the "catching of disease" and such terrible words as "hemophilia" which literally means love of blood.

American readers will be especially interested in a paragraph dealing with American usage which I quote in full:

"American usage differs from ours in the following ways: (1) Reversal of *r* and *e*; *fiber* for *fibre*. Our usage is better. (2) Suppression of *u* after *o* in such words as *color for colour, humor* for *humour*. This is more correct, but our forms are too firmly established to be changed. (3) Suppression of the final *al* after *ic; physiologic* for *physiological*. This again is more correct, since *al* is redundant, but the position is complicated by the conversion of many adjectives ending in *ic* into nouns: *logic, economics*. Note that *economic* and *economical* have different meanings. (4) The use of *e* instead of the ligatures *æ* and *œ* (wrongly called diphthongs). The ligature is a clumsy device and causes great difficulty to typists. Moreover, *oe* fails to represent the original sound *oi*. The Gr. *oisophagos* was represented better by the Early English *ysophagus*. *Fetus* is better Latin than *foetus*. I think the ligatures should be abolished. We get on quite well without them in *economy* (*oikos*, house, *nomos*, law) and similar words. In holding this opinion I find myself in the good company of Fowler."

Note that Dr. Roberts is convinced that the American dropping of the *al* after such words as *physiologic* is more correct since *al* is redundant. Dr. Roberts' conclusion is that, despite occasional lapses and the inevitable inclusion of technical jargon, medicine has developed in its language an instrument of remarkable efficiency.

Somewhat at variance with the opinion of Dr. Roberts is that of Professor Young who emphasizes particularly the weakness of medical language in dealing with the progress of study of the nervous system. Neurologists lean particularly on language in diagnosis of the complicated conditions affecting the brain which concern them. The difficulty lies not in the names that are given to portions of the body but in the manner in which the body works which is function or physiology. Seldom, if ever, does a doctor diagnose the condition by saying, "I am afraid there is something wrong with the organization of your nucleoproteins." He is much more concerned with the ability of the tissue to function as a whole. To quote Dr. Young, "At present many physiologists make observations on nerve impulses and the excitation of one nerve cell by another." Scientists make their descriptions of phenomena by comparisons with behavior. Thus the concept of the brain has it sending messengers or stimuli down the nerves exactly as the heart pumps blood to the large vessels, yet it seems not quite certain that this is just what the brain does in relationship to nerves. Early observers knew nothing of the electrical activities of nerves. As Dr. Young has written, "Every part of a nerve-fibre depends on its cell body, and certainly some entity passes down the fibre to maintain its trophic integrity."

Actually the breaking up of a nerve fiber during degeneration is not fully understood nor is it known how the fiber maintains its

normal cylindric shape; what moves along the nerve fiber may be a change in molecular orientation. The degeneration of a nerve fiber spreads away from a cut surface toward the periphery. Thus a purely electric view is not sufficient to explain what happens in the function of the nervous system.

The question naturally arises how language is to be improved and modified without much more exact knowledge as to how the nervous system functions. Dr. Young concludes that "All our talk of neurons, action potentials, and synaptic transmitters has not produced a satisfactory set of methods for dealing with nervous disease. But it has provided a set of words with which we can at least speak somewhat better than a hundred years ago."

MORRIS FISHBEIN

1. Young, J. Z.: The influence of language on medicine. Lancet. March 28, 1953, pp. 607-611.
2. Roberts, Franccon: Lingua medica: A study in medical semantics. Brit. M. J., June 27, 1953, pp. 1444-1447.

THE DESTRUCTION OF TRICHINA LARVAE

Previous studies have shown that a dose of 750,000 r kills trichina larvae in vitro. A dose of approximately 5000 r inhibits the maturation of larvae to adult forms. A dose of approximately 3500 r produces sexual sterility of adult forms that mature from irradiated larvae.

Now comes a further report by Drs. H. J. Gomberg and S. E. Gould[1] of the radiation dose from a cobalt-60 source that will produce the same effects. The cobalt source at the University of Michigan is derived from an activity devoted to research on the use of radioactive fission byproducts supported by the U. S. Atomic Energy Commission and the Michigan Memorial-Phoenix Project. The studies show that it is possible by irradiation to prevent larvae from maturing even though the larvae show normal motility in the warm-stage test. When trichinous muscle was irradiated, 18,000 r reduced maturation to less than 1 per cent. Radiation dosages required to kill were also determined and it was shown that complete kill requires 750,000 r.

Work is continuing on the irradiation of pork as a possible method of controlling trichinosis. The investigations have shown that undesirable flavor changes occur in many foods when preserving doses are applied. However, one-hundredth of that dose, which is about 2,000,000 r, has resulted in negligible flavor changes.

In May 1952, an outbreak of trichinosis occurred in Glamorgan in England in which at least 25 people were affected as a result of eating pork sausage meat.[2] The infected pigs came from a district which had been incriminated on 6 previous occasions, resulting in 47 human cases. The infected meat was traced back to pork butchers and through them to 1 of 3 sows from a small farm. Live *Trichinellae* were demonstrated in rats and pigs from the suspected farm. In the investigation, a new digestion technic for demonstrating *Trichinellae* in muscles was developed. This method makes use of both peptic and tryptic digestion of muscle fibers and leaves the larvae still motile.

A feature of trichinosis in England is the low mortality contrasted with a case fatality rate of from 16 to 30 per cent in Germany and from 3 to 10 per cent in the United States. The British investigators believe that this is due to the fact that pork is not eaten raw in Great Britain and that the infecting dose is smaller.

In previous editorials in *Postgraduate Medicine*, attention has been called to the significant research of Dr. Gould and his associates at the University of Michigan who are doing basic work in attempting to overcome this hazard. The work here reported is an example of the use of new and modern methods both in the study and in the prevention of trichinosis.

MORRIS FISHBEIN

REFERENCES

1. Gomberg, H. J. and Gould, S. E.: Effects of irradiation with cobalt-60 on Trichina larvae. Science 118:75 (July 17) 1953.
2. Evans, A. D. and Lennox, M.: An outbreak of trichiniasis in Barry, Glamorgan. Brit. M. J. 2:131-134 (July 18) 1953.

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Recommended dosage is 2 to 3 mg./lb. (4.5 to 6.5 mg./Kg.) at four to six-hour intervals. Thus, one teaspoonful every four to six hours for a 50-pound child. Can be administered before, after or with meals. *Pediatric* ERYTHROCIN Stearate Oral Suspension, representing 100 mg. of ERYTHROCIN per 5-cc. teaspoonful, is supplied in 2-fluidounce, pour-lip bottles. Abbott

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THE MEDICAL *Bookman*

► AN ATLAS OF SURGICAL EXPOSURES OF THE EXTREMITIES

By Sam W. Banks, M.D., Associate Professor of Orthopedic Surgery, and Harold Laufman, M.D., Associate Professor of Surgery and Director of Experimental Surgery, Northwestern University Medical School, Chicago. 391 pages with 552 illustrations on 179 plates. 1953, W. B. Saunders Company, Philadelphia & London. $15.00.

One aspect of surgery, somewhat delayed in its fulfillment, is that related to proper surgical approaches. Many textbooks faithfully describe the technic of an operative procedure based on accepted incisional lines. However, it has become increasingly difficult to obtain a comprehensive volume that delineates surgical exposure when normal routine must be interrupted.

With broad perspective the authors have catalogued an all-inclusive compilation that will tend to expedite this previously neglected feature. The basis for proper surgical approach is, of necessity, defined by retention of function in the extremity. The surgeon must gain access to the lesion, remove or repair it, and retreat without permanently offending adjacent vital structures.

The creation, therefore, of such a publication, if it is to have conviction, requires a comprehensive knowledge of laboratory anatomy and profound postoperative success.

One outstanding feature is the communicativeness. All dissections were made on cadavers with each step being accurately photographed. Following this, the structures were labeled and precise dimensional drawings obtained. The descriptive text is meager, but each operative advance is silhouetted so that its perusal becomes leisurely. All features are given adequate consideration. The prevision of the authors in recognizing the necessity for such a volume is noteworthy.

H. O'P.

► PATHOLOGY OF THE HEART

By S. E. Gould, M.D., Clinical Professor of Pathology, Wayne University College of Medicine, Detroit, Michigan, and collaborators. 1,023 pages with 690 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $25.50.

Advances in pathology in general have made it necessary to have special volumes devoted to specific organs or fields. In this volume on the pathology of the heart, a number of eminent collaborators have united to produce the work. The staff work has been excellent, with effective liaison, so that there are few or no omissions and remarkably little repetition or duplication.

Each chapter is well done, which means that it is impossible to select any one for special notice. The first 3 chapters (200 pages) are devoted to the embryologic aspects and the structure and function of the heart. The other chapters present adequate clinical discussions which should appeal to internists. There are many well selected references at the end of each chapter. Due to current interest in the new developments on surgery of the heart, the fields of congenital malformations and rheumatic valvular lesions will be of interest and help to surgeons interested in this branch of surgery.

From the foreword by Karsner to the clinicopathologic correlations by G. B. Myers, valuable information for all interested in diseases of the heart will be found. The last chapter, on gross examination of the heart, alone will appeal to pathologists only.

Illustrations, both gross and microscopic, as well as line drawings, are abundant; they are well chosen and reproduced. In a few, a larger size might add to the attractiveness of the volume.

The paper is very good, the type face is large and clear and few errors were encountered. This book can be highly recommended to serious students of diseases of the heart.

J. W. K.

(Continued on page A-70)

PHOTOGRAPH BY RUZZI GREEN

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► DIABETIC MANUAL FOR THE DOCTOR AND PATIENT

By Elliott P. Joslin, M.D., Clinical Professor of Medicine, Emeritus, Harvard Medical School, Boston. Ed. 9. 315 pages with 55 figures. 1953, Lea & Febiger, Philadelphia. $3.00.

With the current ninth edition, Dr. Joslin's Diabetic Manual for Doctor and Patient continues to provide valuable advice and suggestions as well as answers to most of the practical considerations of the care and regulation of the diabetic patient.

This book provides material for a complete course in training the diabetic. Diet, insulin dosage and administration, special hygiene and many other facets of diabetic self-care are considered in detail.

In addition, problems often posed by the diabetic patient are discussed, such as the role of heredity, marriage, children, diabetic costs, and of course prognosis. In general the book strikes an optimistic note and stresses the importance of meticulous care for successful diabetic management.

T. B. C.

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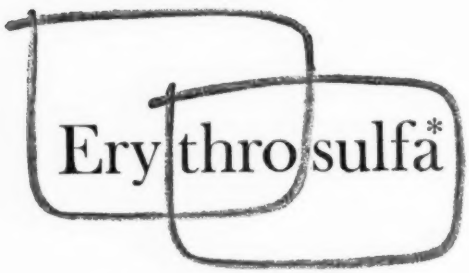

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► CORNELL CONFERENCES ON THERAPY

Editor: Harry Gold, M.D. Editorial Board: David P. Barr, M.D., McKeen Cattell, M.D., Frank C. Ferguson, Jr., M.D., Frank Glenn, M.D. and George Reader, M.D. Vol. 6. 287 pages. 1953, The Macmillan Company, New York. $4.00.

This year's collection of clinical conferences comprises a timely selection of 15 subjects concerning which there have been recent interest and ready application in daily practice. Presentations adhere to the established plan of a short introductory statement of present scientific knowledge and current clinical problems on the subject, followed by a question-answer period and concluded by a summary of the conference findings.

The conference on the use of drugs and radiation in the treatment of leukemia was excellent. It included a short discussion of the pertinent action of the different agents used in the treatment of leukemia, indications for their employment and problems encountered in their use. With the wide use of antibiotics in medicine, the conference on the use of combinations of antibiotics was very informative with regard to such factors as antagonism, synergism, susceptibility and resistance of organisms, and the proper selection of antibiotic agents in specific cases. The place of ion exchange resins in clinical medicine was thoughtfully and impartially reviewed in a good session on that subject.

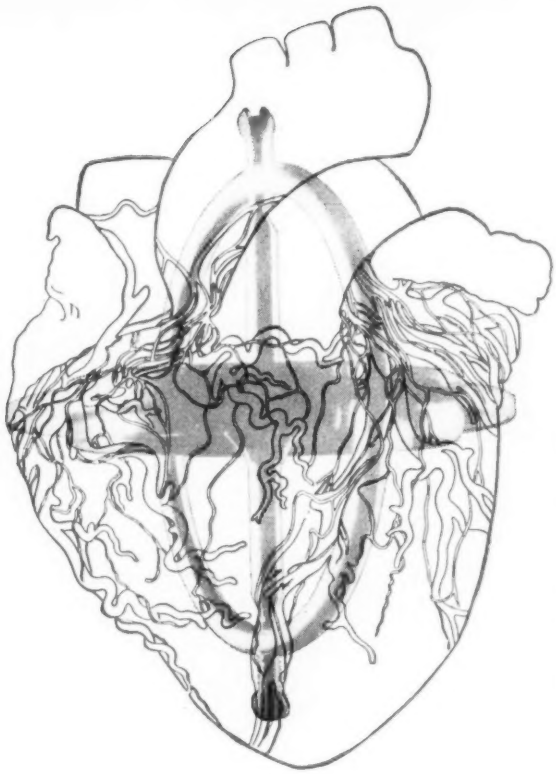
A number of problems relating to the treatment of burns, including treatment of shock, infection, plastic surgery, fluid shifts from one body compartment to another, the place of ACTH in the acute stages of burns and other aspects of treatment were simply and clearly stated in the conference. It was one of the best recent résumés of the modern thinking on burn management by a group of experts working in this field.

Conferences on the treatment of some types of hypertension, bacterial endocarditis, the patient in coma, and osteoporosis were among the better ones presented.

On the whole, this edition is a valuable addition to a series that has earned a well-deserved and important place on the shelf of the general practitioner.

H. C. L.

(Continued on page A-72)



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► THERAPEUTICS IN INTERNAL MEDICINE

Edited by Franklin A. Kyser, M.D., Assistant Professor of Medicine, Northwestern University Medical School, Chicago. Ed. 2. 830 pages. 1953, Paul B. Hoeber, Inc., New York. $15.00.

Although published as a second edition, this is actually a new book. The sections in the first edition have been almost completely rewritten, and 12 new sections and 17 new contributors have been added.

As this is strictly a treatise on treatment, the clinician should know his diagnosis before referring to this work. Descriptions of diseases are not given, and primary surgical methods are not included. Neurologic and dermatologic aspects of diseases observed by internists are presented.

A compendium of this kind cannot be reviewed in the usual manner. Suffice it to say that this volume has complete therapeutic information on every disease in the field of internal medicine, including drugs, diets, physical therapy, hormones, antibiotics, etc. Only a list of the 84 collaborators would indicate the scope of this text.

J. B. C.

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► THE SURGERY OF INFANCY AND CHILDHOOD; Its Principles and Techniques

By Robert E. Gross, M.D., William E. Ladd Professor of Children's Surgery, The Harvard Medical School, Boston. 1000 pages with 1,488 illustrations on 567 figures. 1953, W. B. Saunders Company, Philadelphia & London. $16.00.

In 1941, Ladd and Gross' "Abdominal Surgery of Infancy and Childhood" constituted a major contribution to pediatric surgery. In this new volume Dr. Gross has accomplished a seemingly superhuman task in assembling a comprehensive text covering major surgical procedures in children.

The author has drawn on his vast experience as a surgeon and on the record of surgical procedures through the years at the Children's Medical Center in Boston. The work obviously could not represent the efforts of one man; rather, it is a skilful blending of the author's personal experience with that of his colleagues.

Congenital, inflammatory and neoplastic diseases are included in this book. Surgery of the gastrointestinal tract, thorax, genitourinary tract and cardiovascular system is excellently presented and lucidly written. It is no surprise that the chapters devoted to the surgery of congenital heart disease are outstanding, since Dr. Gross has already established himself as one of the foremost cardiac surgeons.

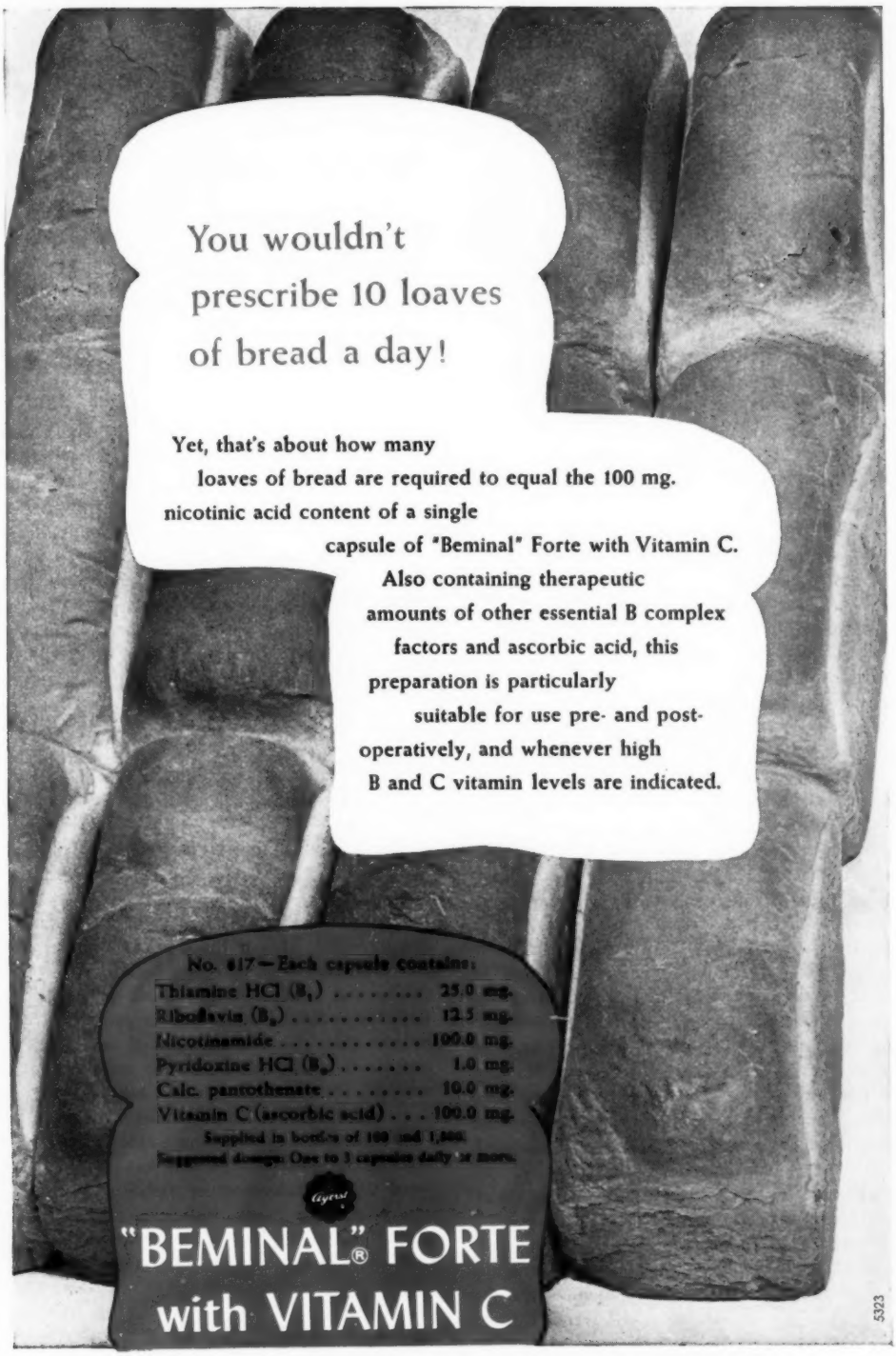
The text is profusely illustrated with excellent photographs and fine drawings. The use of statistical tables in each section is a testimonial to the skill of Dr. Gross and his group.

The author is to be commended for his emphasis on the psychologic preparation of children for hospitalization and operation. He offers many practical hints on such topics as the parenteral administration of fluids, bedside apparatus and nursing technics. Great progress in pediatric surgery is reflected in the presentation of the modern approach to the repair of esophageal atresia and imperforate anus. The results of the combined surgery and irradiation treatment for Wilms's tumor are encouraging.

Although there may be justifiable criticism of the author's stand in various instances, over all, the book is excellent and represents a notable achievement by Dr. Gross and his staff.

E. C. B.

(Continued on page A-74)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► MID-CENTURY PSYCHIATRY

Edited by Roy R. Grinker, M.D., Director, Institute for Psychosomatic and Psychiatric Research and Training, Michael Reese Hospital, Chicago. 183 pages. 1953, Charles C Thomas, Springfield, Illinois. $5.50.

Following the introduction by Dr. Grinker, this symposium begins with a discussion by Dr. Percival Bailey of the University of Illinois on the "cortex and mind" from an anatomic and evolutionary standpoint. Dr. Bailey points out that consciousness is the elusive function that as yet remains unlocalized.

Dr. Ralph Gerard of the University of Illinois considers current neurophysiologic concepts in their relation to behavior, and Dr. George Engel of the University of Rochester presents a broad conceptual scheme considering the defense mechanisms of the body as quantitative variables in a unitary concept of health and disease.

Dr. David Shakow of the University of Illinois examines the historical aspects of experimental psychology and brings out the points of progress and obstruction in the field. Next follows a presentation of a classic analysis of the instinctual energies that form the personality of the individual, by Dr. Therese Benedek.

The opinion is expressed by Dr. Howard Liddell of Cornell University that we have been too much interested in the problems of stress and disease, and he feels that perhaps we could gain a great deal by determining the source and uses of hopes and pleasures.

Interesting data are offered by Dr. David Levy of Columbia University illustrating methods of "observational psychiatry" as a technic.

Dr. Ralph Kaufman of Columbia University recapitulates the current conceptual schemes in psychoanalysis, and Dr. Thomas French of the Chicago Analytical Institute states that the psychoanalytic method of attributing importance to arbitrary divisions of the personality for the understanding of the patient is no longer productive. The possible ways in which the social sciences have influenced psychiatry are examined by Dr. Charles Johnson of Fiske University.

Dr. Franz Alexander of the Chicago Analytical Institute details the therapeutic applications of psychoanalysis and its derivatives, and Dr. John Spiegel of the Michael Reese Hospital presents a brief and lucid summary of the symposium.

R. H. K.

► ROENTGEN, RADIUM AND RADIOISOTOPE THERAPY

By A. J. Delario, M.D., Head of Therapeutic Radiology, St. Joseph Hospital, Paterson, New Jersey. 371 pages with 65 illustrations and 155 tables. 1953, Lea & Febiger, Philadelphia. $7.50.

In recent years great advances have been made by the radiation physicists in development of new tools for radiation therapy. This advance has been spurred by the production of radioactive isotopes through the atomic energy program. Another stimulating force has been the development of multiple methods of producing high energy or supervoltage x-rays. A large volume of literature describing these developments has been collected over a period of years and there has been a definite need to accumulate this knowledge in a textbook with reference sources for the student.

In compiling such a text emphasis must necessarily be placed on certain subjects, and other areas of study, therefore, receive less careful attention. The portions of the book dealing with the physics of radiation and some of the biologic changes of radiation, especially of the injuries caused by ionizing radiation, appear complete. However, the author has included some personal theories as to the generation of x-rays and their reactions for which there is no supporting evidence given.

The author includes a short chapter on diseases amenable to radiation therapy and the radiation dose. This chapter is a bare outline of the diseases that have been treated with radiation, and no important details of the disease processes and the expected therapeutic response are included. This is the weakest portion of the text and should be so recognized by the reader.

The last portion of the book concerns itself with the radioactive substances produced by the atomic pile. A great volume of information is contained herein and again the references to the original source work are well tabulated and the sources have been carefully selected.

The text can be recommended for collateral reading for a radiologist who has primarily mastered the fundamentals of radiation so that he can select the basic well-supported ideas expressed therein and reject controversial ideas that are not supported by adequate evidence.

J. F.

(Continued on page A-76)

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► TUMORS OF THE ORBIT AND ALLIED PSEUDO TUMORS

An Analysis of 216 Case Histories. By Raymond G. Ingalls, M.D., Former Instructor in Ophthalmology, College of Physicians and Surgeons, Columbia University, New York. 410 pages with 153 illustrations. 1953, Charles C Thomas, Springfield, Illinois. $11.50.

An analysis of 216 case histories of orbital tumors originally assembled for exhibition at the 1947 meeting of the American Academy of Ophthalmology and Otolaryngology comprises this text. The greater part of the material used was obtained from the Pathology Laboratory of the Institute of Ophthalmology of the Presbyterian Hospital. The pathologic material was classified on an oncologic basis. The general plan of the book consists of tables showing history and chief complaint, location within the orbit and other clinical symptoms. These tables apply only to the cases included in this analytic report and are not consistently comparable to reports of other series. A brief synopsis of current literature on each kind of tumor is added in each chapter. The illustrations are very good and well selected. None are in color. The book is valuable for ready reference, contains interesting factual data, and will be particularly useful to ophthalmologic and neurologic surgeons.

W. L. B.

Books received will be acknowledged in this department each month. As space permits, books of principal interest to our readers will be reviewed more extensively.

Modern Concepts in Medicine. By Julius Jensen, Ph.D. (In Medicine), University of Minnesota. 636 pages, illustrated. 1953, The C. V. Mosby Company, St. Louis. $11.50.

Effective Inhalation Therapy. By Edwin Rayner Levine, M.D., Chairman, Committee on Physiologic Therapy, American College of Chest Physicians, with the cooperation of Alvan L. Barach, M.D., J. Winthrop Peabody, M.D. and Maurice S. Segal, M.D. 157 pages, illustrated in color. 1953, National Cylinder Gas Company, Chicago. $4.50.

Health and Human Relations. Report of a conference on Health and Human Relations held at Hiddesen near Detmold, Germany, August 2-7, 1951. Sponsored by The Josiah Macy, Jr. Foundation, New York City. 192 pages. 1953, The Blakiston Company, Inc., New York & Toronto. $4.00.

Emotional Factors in Skin Disease: A Psychosomatic Medicine Monograph. By Eric Wittkower, M.D. and Brian Russell, M.D., with contributions from Peter Edgell, Desmond Irwin and John Slorach. 214 pages. 1953, Paul B. Hoeber, Inc., New York. $4.00.

Diseases of the Liver, Gallbladder and Bile Ducts. By S. S. Lichtman, M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College, New York. Ed. 3. 1,315 pages with 220 illustrations and 3 color plates. 2 volumes. 1953, Lea & Febiger, Philadelphia. $22.00.

Survey of Antimalarial Agents: Chemotherapy of Plasmodium Gallinaceum Infections; Toxicity; Correlation of Structure and Action. By G. Robert Coatney, Ph.D., W. Clark Cooper, M.D., Nathan B. Eddy, M.D. and Joseph Greenberg, Ph.D. 323 pages. Public Health Monograph No. 9. 1953, United States Government Printing Office, Washington, D.C. $1.25.

Mechanisms of Urologic Disease. By David M. Davis, M.D., Professor of Urology Emeritus, Jefferson Medical College and Visiting Lecturer in Urology, Graduate School of Medicine, University of Pennsylvania, Philadelphia. 156 pages. 1953, W. B. Saunders Company, Philadelphia and London. $4.50.

The Pharm-Assist Manual (Formerly Gray's Pharmaceutical Quiz Compend). Completely rewritten by A. E. Slesser, Ph.D., Professor of Pharmacy, Head of the Department of Pharmacy, and Assistant to the Dean, University of Kentucky College of Pharmacy, Louisville, Kentucky. 167 pages. 1953, The C. V. Mosby Company, St. Louis. $3.50.

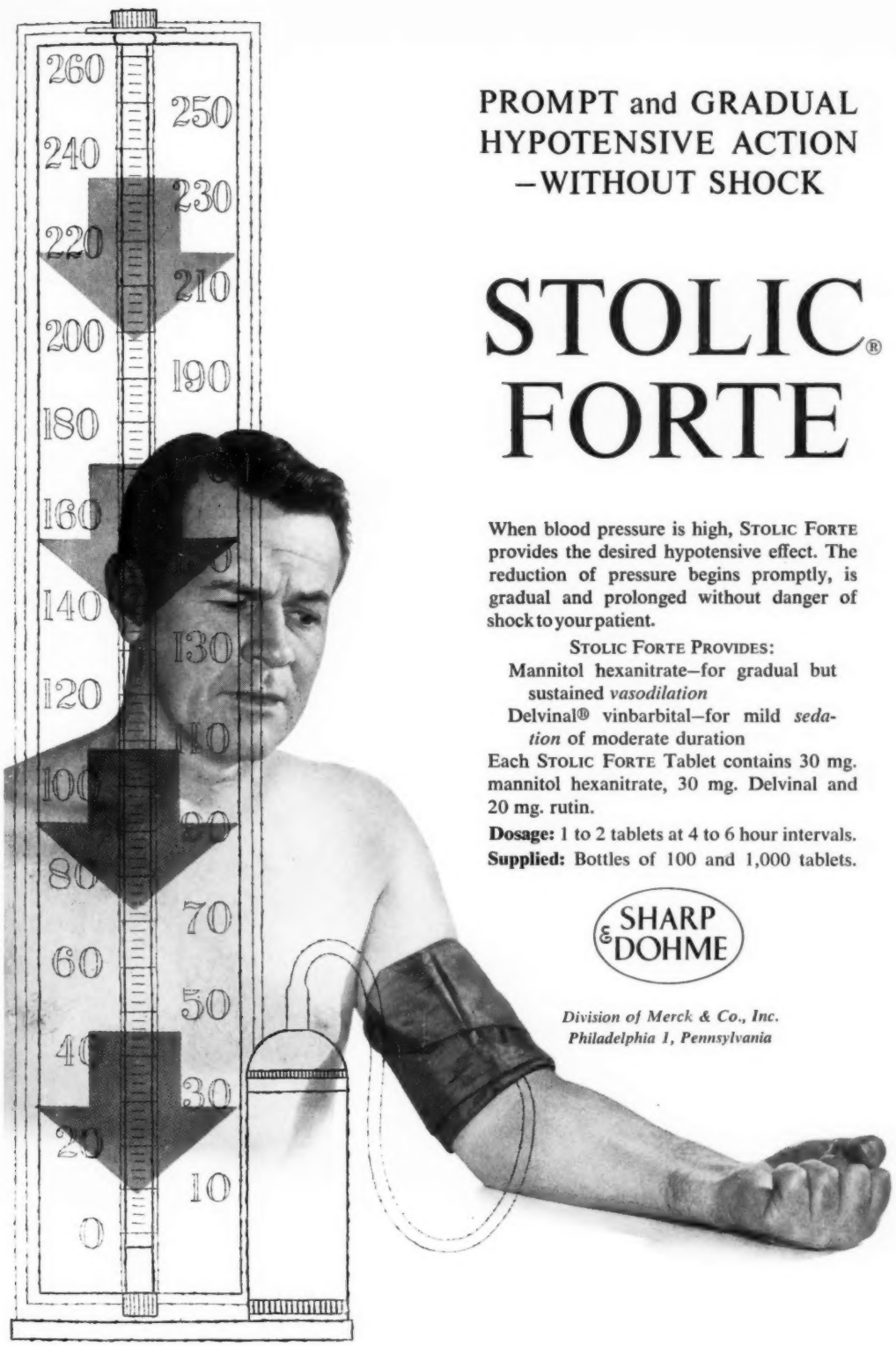
Experimental Atherosclerosis. By Louis N. Katz, M.D. and Jeremiah Stamler, M.D., Cardiovascular Department, Medical Research Institute, Michael Reese Hospital, Chicago, Illinois. 375 pages with 46 illustrations and 84 tables. 1953, Charles C Thomas, Springfield, Illinois. $10.50.

Differential Diagnosis of Common Diseases of the Eyeground. By Paul Tower, M.D., Los Angeles, California. 243 pages with 129 figures. 1953, Grune & Stratton, New York. $10.00.

Classics in Clinical Dermatology; With Biographical Sketches. By Walter B. Shelley, M.D., Chief, Clinic of Dermatology, University of Pennsylvania Hospital, and John T. Crissey, M.D., Instructor, Dermatology and Syphilology, University of Pennsylvania, Philadelphia. 467 pages with 107 figures. 1953, Charles C Thomas, Springfield, Illinois. $10.50.

Endocrinology in Clinical Practice. Edited by Gilbert S. Gordan, M.D., Assistant Professor of Medicine, University of California School of Medicine and H. Lisser, M.D., Clinical Professor of Medicine and Endocrinology, University of California School of Medicine. 407 pages, illustrated. 1953, The Year Book Publishers, Inc., Chicago. $10.50.

It's Not All in Your Mind. By H. J. Berglund, M.D. and H. L. Nichols, Jr. 343 pages. 1953, North Castle Books, Greenwich, Connecticut. $3.95.



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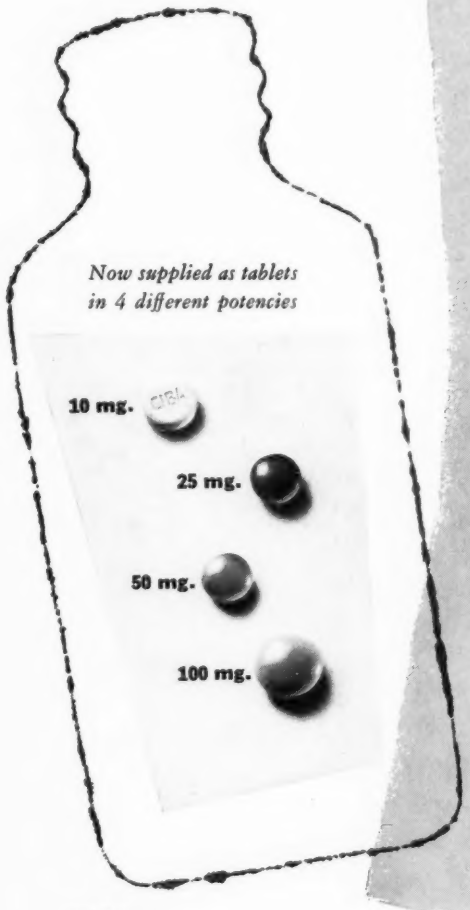

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